

A GUIDEBOOK TO
**MECHANISM
IN ORGANIC
CHEMISTRY**

SIXTH EDITION



PETER SYKES

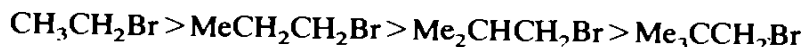
13

Linear free energy relationships

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13.1 INTRODUCTION

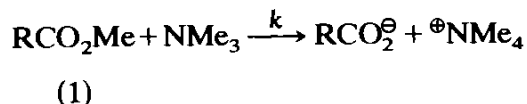
In previous chapters we have considered the relative reactivity of numerous series of compounds in specific reactions—such as nucleophilic displacement by EtO^\ominus in the series of bromoalkanes below (cf. p. 86)—



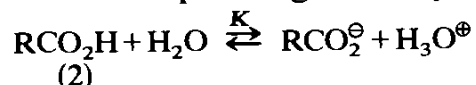
and have sought to account for the reactivity sequences observed in terms of the operation of electronic and steric effects. This has proved a useful and rewarding exercise, but a major disadvantage of such studies, and explanations, is that they remain *qualitative*: what is still needed is a method for relating structure and reactivity on a *quantitative* basis.

13.2 FIRST HAMMETT PLOTS

The first such relationship, on a thoroughly established basis, was observed by Hammett as long ago as 1933. He showed that for the reaction of a series of methyl esters (1) with NMe_3 ,



the rates of reaction were directly related to the ionisation constants, in water, of the corresponding carboxylic acids (2):



Thus on plotting $\log k$ for reaction of the esters (1) against $\log K$ for ionisation of the acids (2) (he actually plotted the $-\log$ values so as to have more easily handled numbers) a reasonable straight line resulted (Fig. 13.1):

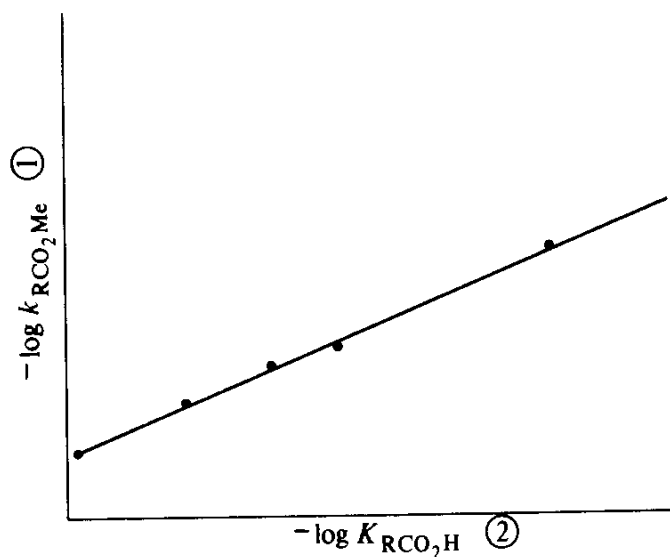


Fig. 13.1

Equilibrium constants, K , and rate constants, k , are each related to free energy changes (pp. 34, 38) in the relevant reactions in the following way:

$$\log K = \frac{-\Delta G^\ominus}{2.303 RT}$$

$$\log k = \frac{-\Delta G^\ddagger}{2.303 RT} + \log \left[\frac{k'T}{h} \right]$$

$$\left[\begin{array}{l} k' = \text{Boltzmann's constant} \\ h = \text{Planck's constant} \end{array} \right]$$

The fact that there is in Fig. 13.1 a straight line relationship between $-\log k$ for reaction of the esters (1), and $-\log K$, for ionisation in

water of the corresponding carboxylic acids (2), implies that there is also a straight line relationship between ΔG^\ddagger , the free energy of activation for the ester reaction, and ΔG^\ominus , the standard free energy change for ionisation in water of the acids. Because of this straight line relationship between the free energy terms for these two different reaction series, straight line plots like the one in Fig. 13.1 are generally referred to as *linear free energy relationships*.

Another early example of Hammett's is shown in Fig. 13.2, which represents a plot of $\log k$ for base-catalysed hydrolysis of a group of ethyl esters (3) against $\log K$ for ionisation in water of the corresponding carboxylic acids (2). Judged

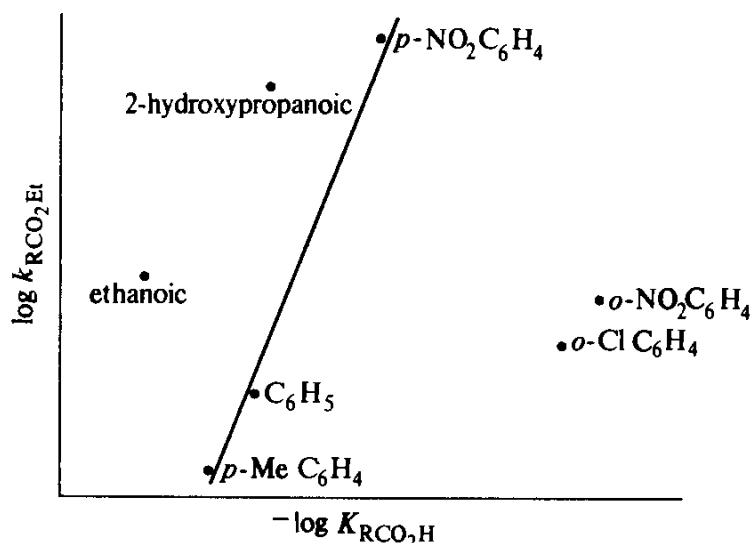
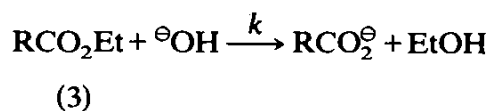


Fig. 13.2

by the standards of Fig. 13.1, the plot in Fig. 13.2 is pretty disappointing: there is a straight line relationship for benzoic acid and its $p\text{-Me}$ and $p\text{-NO}_2$ derivatives, but the $o\text{-NO}_2$ and $o\text{-Cl}$ benzoic acid derivatives then lie far off to one side of this straight line, while the aliphatic derivatives, of ethanoic and 2-hydroxypropanoic acids, lie far off to the other side. Hammett found indeed that straight lines were not generally obtained if reaction data for either o -substituted benzene derivatives, or aliphatic species, were included in the plot. He did, however, find that if consideration was restricted to reactions of m - and p -substituted benzene derivatives, then—as shown for ester hydrolysis in Fig. 13.3 (p. 361)—excellent linearity resulted, and this held for a very wide range of different reactions of such derivatives.

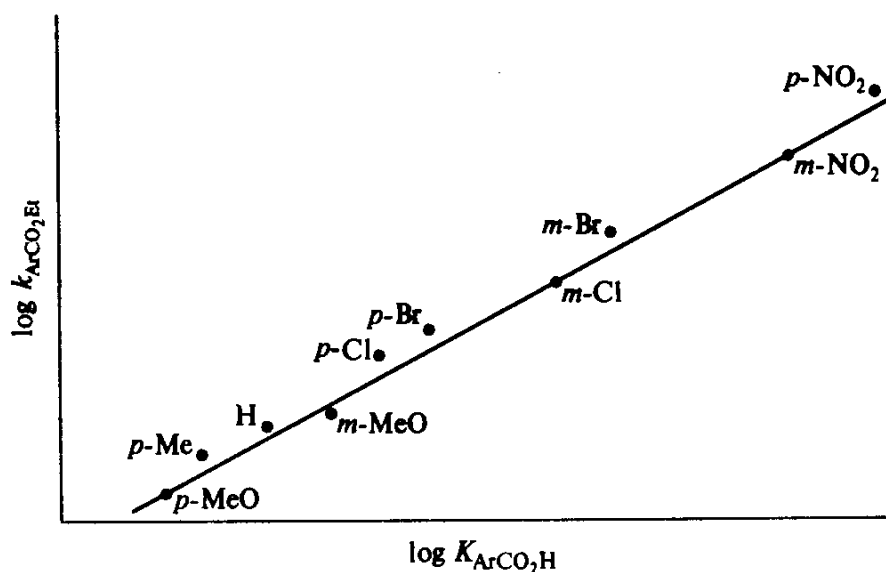
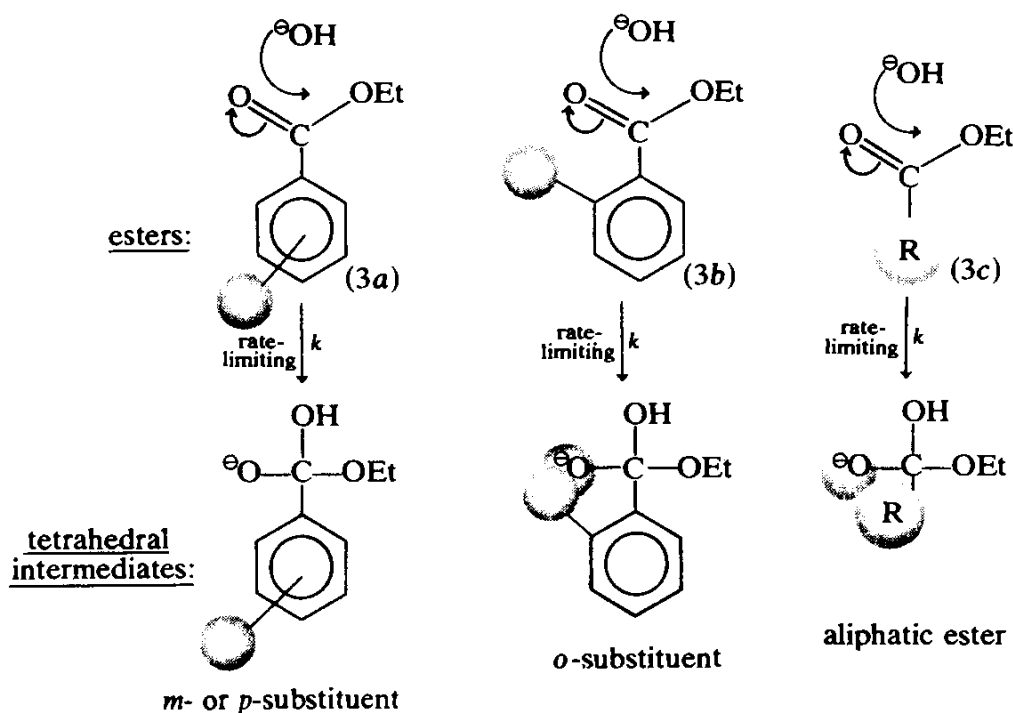


Fig. 13.3

A reason for such non-conformity on the part of *o*-substituted benzene, and of aliphatic, derivatives is not far to seek. Thus for the base-catalysed hydrolysis (p. 238) of the esters (3) in Figs 13.2 and



13.3, the *m*- or *p*-substituent in (3a) is far removed from the reaction centre and, in this rigid molecule, can exert no steric effect upon it. By contrast, the *o*-substituent in (3b) is close at hand (cf. p. 242), and leads to increasing crowding in the transition state leading to the tetrahedral intermediate produced in slow, rate-limiting attack on ester (3b) by $^{\ominus}\text{OH}$; very much the same is true also for the

more flexible molecules of the aliphatic ester (3c). Such steric effects will be much smaller, if indeed apparent at all, in the removal of the peripheral H from the CO₂H group by H₂O (i.e., in acid ionisation).

13.3 THE HAMMETT EQUATION

Despite establishing such linear relationships for a wide range of reactions of *m*- and *p*-substituted benzene derivatives, we still lack any simple form of this quantitative relationship that can actually be used to investigate new situations: here again, it was Hammett who supplied the answer.

13.3.1 Derivation of Hammett equation

The general equation for a straight line is $y = mx + c$, and this can be applied to the straight line in Fig. 13.3 to give,

$$\log k_X = \rho \log K_X + c \quad [1]$$

where ρ is the slope of this straight line, c the intercept, and X is the particular *m*- or *p*-substituent in the benzene ring of the species concerned. It is also possible to write an exactly analogous equation that is restricted to the *unsubstituted* ester and acid, i.e. where X = H:

$$\log k_H = \rho \log K_H + c \quad [2]$$

Subtracting [2] from [1], we obtain,

$$\log k_X - \log k_H = \rho(\log K_X - \log K_H) \quad [3]$$

which may also be written in the form:

$$\log \frac{k_X}{k_H} = \rho \log \frac{K_X}{K_H} \quad [4]$$

13.3.2 Substituent constant, σ_X

Hammett then designated the ionisation, in water at 25°, of *m*- and *p*-substituted benzoic acids as his *standard reference reaction*. He chose this reaction because reasonably precise aqueous ionisation constant, K_X , data were already available in the literature for quite a range of differently *m*- and *p*-substituted benzoic acids. Knowing K_H and K_X for a variety of differently X-substituted benzoic acids, it is then possible to define a quantity, σ_X , as

$$\sigma_X = \log \frac{K_X}{K_H} \quad [5]^*$$

* [5] may, of course, also be written in the form, $\sigma_X = pK_{a(H)} - pK_{a(X)}$; so that the numerical value of σ_X for a particular substituent is obtained by simple subtraction of the pK_a value for the substituted acid (where this is known) from the pK_a value for benzoic acid itself.

where σ_X is a *substituent constant*, whose value will remain constant for a specific substituent in a specific position (*m*- or *p*-), irrespective of the nature of the particular reaction in which a benzene derivative, carrying this substituent, is involved.

Substituting [5] into [4] we then get,

$$\log \frac{k_X}{k_H} = \rho \sigma_X \quad [6]$$

which is the usual form of what has come to be called the Hammett equation.

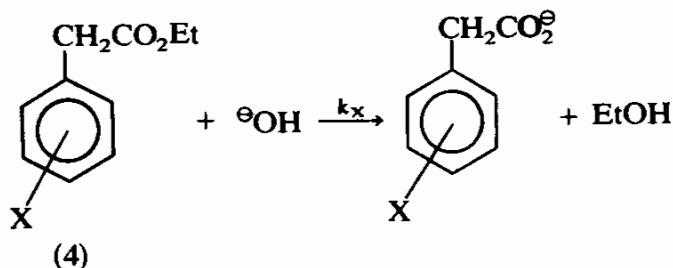
By using known values of K_X (or pK_a) for aqueous ionisation of *m*- and *p*-substituted benzoic acids (or measuring K_X [pK_a] where the value is not already available for a particular *m*- or *p*-substituent) it is possible to calculate σ_X as required, and a selection of values obtained in this way is shown below:

Substituent, X	σ_{m-X}	σ_{p-X}	
Me ₃ C	-0.10	-0.20	
Me	-0.07	-0.17	
H	0	0	(by definition)
MeO	+0.12	-0.27	
HO	+0.12	-0.37	
F	+0.34	+0.06	
Cl	+0.37	+0.23	
MeCO	+0.38	+0.50	
Br	+0.39	+0.23	
CN	+0.56	+0.66	
NO ₂	+0.71	+0.78	

Hardly surprisingly, the value of σ_X for a particular substituent is found to depend on the location of the substituent, having a different value in the *m*-position from that in the *p*-position.

13.3.3 Reaction constant, ρ

Having thus obtained a range of substituent constant, σ_X , values it is now possible to use them to calculate the value of ρ , the *reaction constant*, in [6] for any further reactions in which we may be interested: this is often done graphically. Thus to evaluate ρ for, say, the base-catalysed hydrolysis of *m*- and *p*-substituted ethyl 2-arylethanoates (4) we would, from kinetic measurements (or from



the literature if we're lucky!), obtain k_H for the unsubstituted ester, and k_X for at least three different substituted esters. Knowing the value of σ_X for each of these substituents, we can then plot $\log(k_X/k_H)$ against σ_X and, from [6], the slope of the resulting straight line will be the value of ρ for this reaction: it turns out to be +0.82 for this particular hydrolysis, when carried out in aqueous ethanol at 30°. The ρ values for quite a wide range of different reactions of *m*- and *p*-substituted benzene derivatives are shown below:

Reaction	Type	ρ
(1) ArNH_2 with $2,4\text{-(NO}_2)_2\text{C}_6\text{H}_3\text{Cl}$ in $\text{EtOH}(25^\circ)$	k	-3.19
(2) ArNH_2 with PhCOCl in $\text{C}_6\text{H}_6(25^\circ)$	k	-2.69
(3) ArCH_2Cl solvolysis in aq. $\text{Me}_2\text{CO}(69.8^\circ)$	k	-1.88
(4) ArO^\ominus with EtI in $\text{EtOH}(25^\circ)$	k	-0.99
(5) ArCO_2H with MeOH (acid-catalysed, 25°)	k	-0.09
(6) ArCO_2Me hydrolysis (acid) in aq. $\text{MeOH}(25^\circ)$	k	+0.03
(7) $\text{ArCH}_2\text{CO}_2\text{H}$ ionisation in $\text{H}_2\text{O}(25^\circ)$	K	+0.47
(8) ArCH_2Cl with I^\ominus in $\text{Me}_2\text{CO}(20^\circ)$	k	+0.79
(9) $\text{ArCH}_2\text{CO}_2\text{Et}$ hydrolysis (base) in aq. $\text{EtOH}(30^\circ)$	k	+0.82
(10) ArCO_2H ionisation in $\text{H}_2\text{O}(25^\circ)$	K	+1.00 (standard reaction)
(11) ArOH ionisation in $\text{H}_2\text{O}(25^\circ)$	K	+2.01
(12) ArCN with H_2S (base) in $\text{EtOH}(60.6^\circ)$	k	+2.14
(13) ArCO_2Et hydrolysis (base) in aq. $\text{EtOH}(25^\circ)$	k	+2.51
(14) ArNH_3^\oplus ionisation in $\text{H}_2\text{O}(25^\circ)$	K	+2.73

The standard reaction, the aqueous ionisation of *m*- and *p*-substituted benzoic acids at 25° , will have a ρ value of 1.00 as a necessary concomitant of the definition of σ_X in [5], and its use in [6]. The value of the reaction constant, ρ , for a particular reaction, carried out under specified conditions, remains constant no matter what the *m*- or *p*-substituents present in the compounds involved.

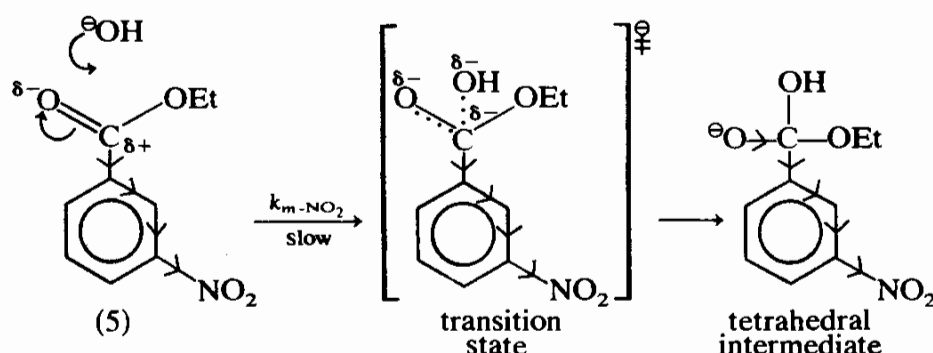
13.3.4 Physical significance of σ_X

Before we can go on to consider the actual use that may be made of Hammett plots, it is necessary to provide some physical justification for σ_X and ρ in terms of the more familiar factors that we have already seen influencing reaction rates and equilibria.

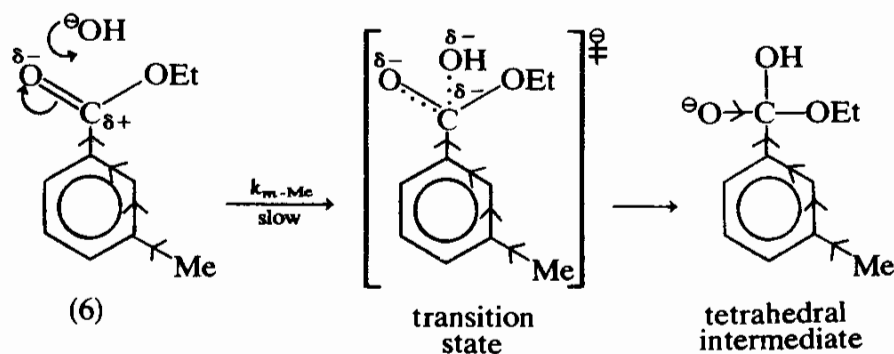
If we consider σ_X , the substituent constant, first and look at the list of σ_{m-X} values (p. 363), we can see that *m*- Me_3C and *m*- Me each have a small -ve value, H has the value—by definition—of zero, while all the other *m*-substituents have (increasing) +ve values. The change in sign (-ve \rightarrow +ve) does, of course, parallel the change in direction (electron-donating \rightarrow electron-withdrawing) of the inductive effect exerted by these substituents. The substituents may also exert a field effect (p. 22), operating through the medium, but this will act in the same direction as the inductive effect. It

would thus seem that σ_{m-X} represents, both in direction and magnitude, a measure of the *total polar effect* exerted by the substituent X on the reaction centre.

This is borne out by a comparison of the rates of base-catalysed hydrolysis (cf. p. 238) of *m*-NO₂ (5), and of *m*-Me (6), substituted ethyl benzoates with that of the unsubstituted ester: a reaction in which the slow, and hence rate-limiting, step is initial attack on the ester by $^{\ominus}\text{OH}$ (p. 239):



$$\sigma_{m-\text{NO}_2} = +0.71 \quad \frac{k_{m-\text{NO}_2}}{k_H} = 63.5$$

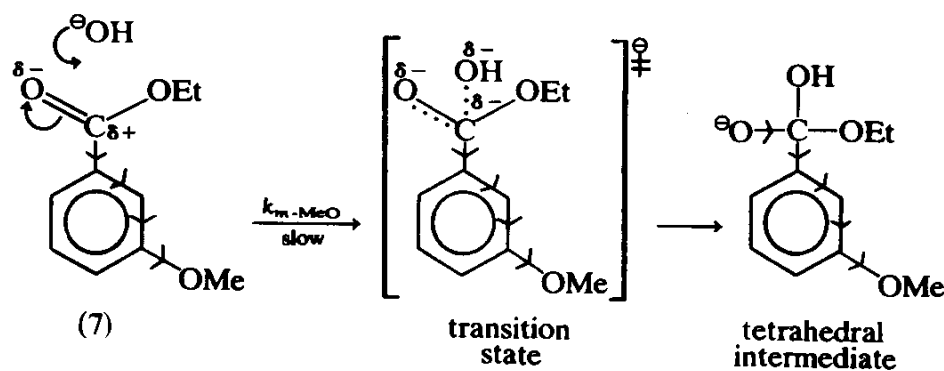


$$\sigma_{p-\text{MeO}} = -0.27 \quad \frac{k_{m-\text{Me}}}{k_H} = 0.66$$

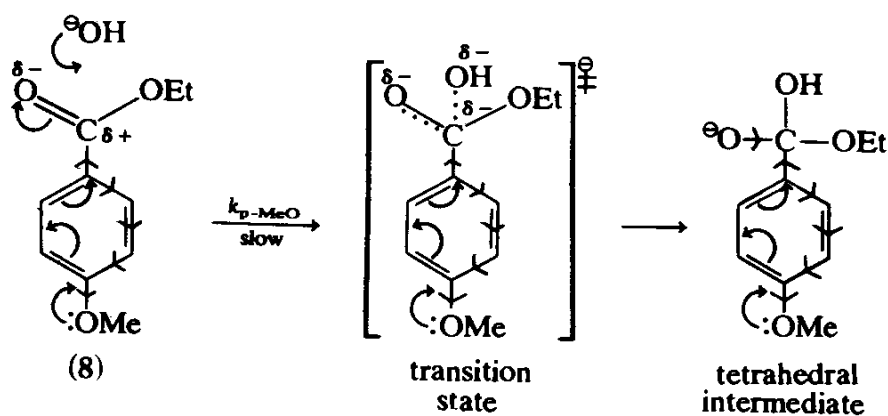
The *m*-nitro ester (5), with $\sigma_{m-\text{NO}_2} = +0.71$, is hydrolysed 63.5 times as fast as the unsubstituted ester (powerful electron-withdrawal markedly assisting $^{\ominus}\text{OH}$ attack on the carbonyl carbon atom, and stabilising the transition state leading to the negatively charged tetrahedral intermediate); while the *m*-Me ester (6), with $\sigma_{m-\text{Me}} = -0.07$, is hydrolysed 0.66 times as fast as the unsubstituted ester (very weak electron-donations slightly inhibiting $^{\ominus}\text{OH}$ attack, etc.).

If we now look at the list of σ_{p-X} values (p. 363), it is apparent that not only does the σ_{p-X} value for a particular substituent, X, vary in *magnitude* from the σ_{m-X} value for the same substituent, it may differ in *sign* too: as is the case with *m*- and *p*-MeO. An examination of the effect of a *m*-MeO (7) and a *p*-MeO (8) substituent on the same reaction as above (base-catalysed ester

hydrolysis) makes plain the reason for this change in sign:



$$\sigma_{m-\text{MeO}} = +0.12 \quad k_{m-\text{MeO}} > k_{\text{H}}$$



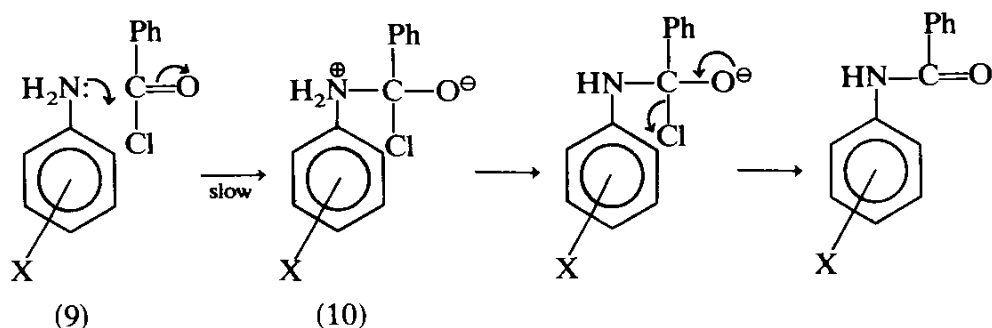
$$\sigma_{p-\text{MeO}} = -0.27 \quad k_{\text{H}} > k_{p-\text{MeO}}$$

In the *m*-position, the electronegative oxygen atom of the MeO group exerts an electron-withdrawing inductive effect ($\sigma_{m-\text{MeO}} = +0.12$) and hydrolysis is faster than with the unsubstituted ester [*cf.* the *m*-NO₂ ester (5)]. In the *p*-position, MeO will still exert an electron-withdrawing inductive effect, but in addition it can, through its electron pairs, exert an electron-donating mesomeric effect on the ring carbon atom to which the CO₂Et group is attached. The latter effect, because it involves the more readily polarisable π electron system, is the greater of the two, and the overall result is therefore *net* electron-donation ($\sigma_{p-\text{MeO}} = -0.27$); as is required by the observation that the *p*-MeO ester is hydrolysed markedly more slowly than the unsubstituted compound (*cf.* p. 154).

Thus σ_{X} can be regarded as a measure of the *overall polar effect* exerted by a substituent, X, on the reaction centre. Its *sign* indicates the *direction* (−ve = electron-donating; +ve = electron-withdrawing), and its *magnitude* the *extent*, of the effect that X exerts—compared, of course, with the effect exerted by H. Indeed, the assumed constancy of a substituent's σ_{X} value, over a wide range of different reactions, does not necessarily imply that the *absolute* polar effect of X always remains constant, but only that its effect *relative* to H remains constant.

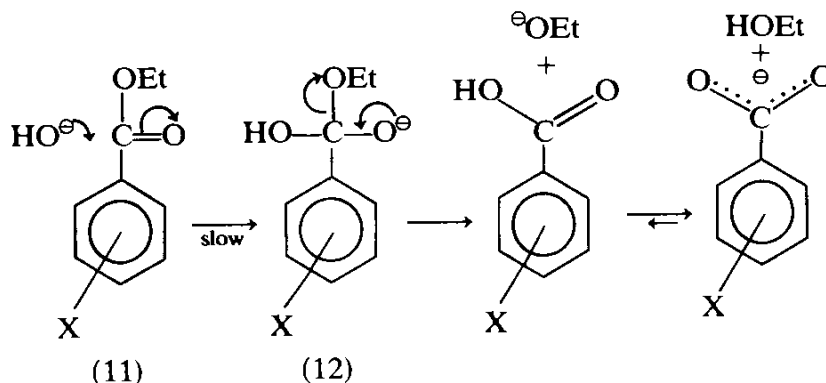
13.3.5 Physical significance of ρ

Now let us consider ρ , the reaction constant. Looking at the list of ρ values (p. 364), we can select first a reaction with a sizeable $-ve$ ρ value, say reaction 2—the benzylation of *m*- and *p*-substituted anilines (9)—with $\rho = -2.69$, and look at this reaction rather more closely:



The slow, rate-limiting step of this reaction is found to be initial attack by the electron pair of the nitrogen atom of the substituted aniline (9) on the carbonyl carbon atom of the acid chloride. This results in the development of $+ve$ charge at the reaction centre—the N atom attached directly to the substituted benzene ring in the forming intermediate (10). The reaction is thus accelerated by electron-donating substituents, which help delocalise this forming $+ve$ charge in the transition state leading to the intermediate (10), and correspondingly retarded by electron-withdrawing substituents; this behaviour is found to hold in general for reactions with $-ve$ ρ values.

We have already had some discussion of a reaction with a $+ve$ ρ value, reaction 13 in the list (p. 364), the base-catalysed hydrolysis of *m*- and *p*-substituted ethyl benzoates (11):



This has ρ value of $+2.51$, the known slow, rate-limiting step in this reaction is attended by the development of $-ve$ charge adjacent to the reaction centre in the transition state leading to the intermediate (12), and the overall reaction is, as we have already seen (p. 365),

accelerated by electron-withdrawing, and retarded by electron-donating, substituents.

Thus ρ can be regarded as a measure of the *susceptibility* of a reaction to the electron-donating or- withdrawing effect exerted by a substituent X; relative, of course, to the susceptibility (towards such a substituent) of the standard reaction—the aqueous dissociation of *m*- and *p*-substituted benzoic acids at 25°—for which $\rho = +1.00$, by definition. The *sign* of ρ is of diagnostic value, as we have seen, in that a -ve value indicates the development of +ve charge (or, of course, the disappearance of -ve charge) at the reaction centre during formation of the T.S. in the rate-limiting step of the overall reaction; while, *vice versa*, a +ve value indicates the development of -ve charge (or the disappearance of +ve charge) at that centre. The *magnitude* of ρ can be regarded, therefore, as a measure of the *change* in charge density at the reaction centre during formation of the T.S., or on proceeding from one side of an equilibrium to the other.

On this basis, it might well be expected that the ρ value, of otherwise similar reactions, would decrease as the reaction centre is moved further away from the substituents that are exerting a polar, electronic effect upon it. This is borne out by the ρ values for the aqueous ionisation of the acids (13)–(16):

Acid ionisation (H ₂ O)	ρ
(13) XC ₆ H ₄ CO ₂ H	1.00 (standard reaction)
(14) XC ₆ H ₄ CH ₂ CO ₂ H	0.49
(15) XC ₆ H ₄ CH ₂ CH ₂ CO ₂ H	0.21
(16) XC ₆ H ₄ CH=CHCO ₂ H	0.47

Introduction of first one, and then two, CH₂ groups between the benzene ring and CO₂H progressively reduces the susceptibility of the acid's ionisation to the polar effect of the substituent X in the benzene ring. The susceptibility, as revealed by the value of ρ , rises again for (16), however, as CH=CH is a markedly better transmitter of electronic effects than is CH₂—CH₂.

13.3.6 Through-conjugation: σ_X^- and σ_X^+

Before we go on to consider the major uses of σ_X and ρ , it is first necessary to take a little closer look at just how constant the σ_X value for a particular substituent really is. If we plot data for the aqueous ionisation of *m*- and *p*-substituted benzoic acids (13)—the standard reaction—against that for ionisation of the corresponding substituted phenols (17), a very reasonable straight line (Fig. 13.4) is

obtained for a wide range of different substituents:

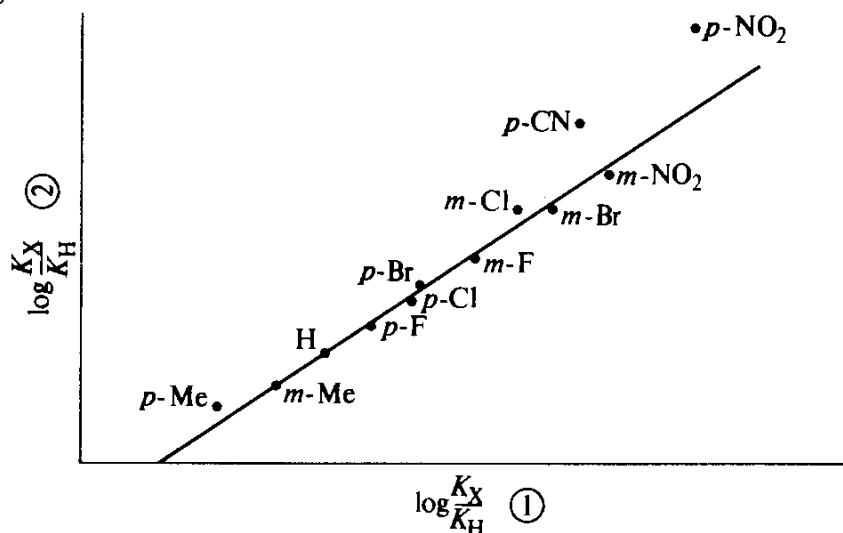
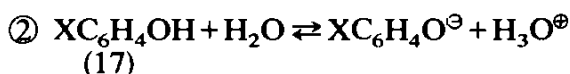
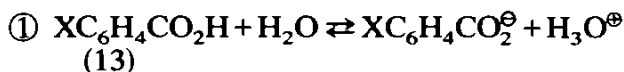
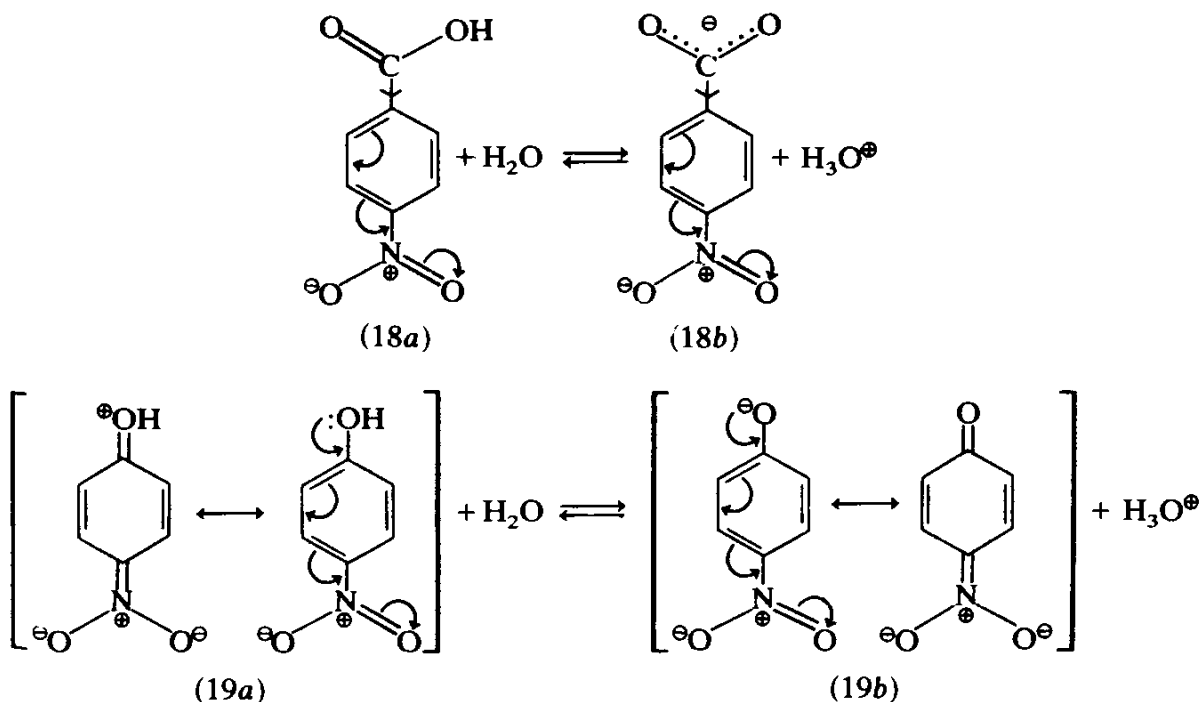


Fig. 13.4

Two substituents however, the powerfully electron-withdrawing $p\text{-NO}_2$ and $p\text{-CN}$, lie *above* this straight line: indicating that $p\text{-NO}_2$ phenol and $p\text{-CN}$ phenol are in fact *stronger* acids than we might have expected them to be. Why this is so becomes apparent if we write out the structures of the species involved in both ionisation equilibria for, say, the $p\text{-NO}_2$ compounds (18 and 19) and examine the polar, electronic effects that can operate in them:



For each species, the inductive effect of the p -NO₂ substituent—which will be essentially similar in each of the sets of species—has been omitted, but the mesomeric or conjugative effect has been included. In (18a) \rightleftharpoons (18b), the standard reaction that was used to evaluate $\sigma_{p\text{-NO}_2}$, the conjugative effect of the p -NO₂ substituent is transmitted ultimately to the reaction centre only through an inductive effect: operating on the CO₂H, or CO₂[⊖], group from the ring carbon atom to which it is attached. In (19a) \rightleftharpoons (19b), however, the conjugative effect can be transmitted right through from the p -NO₂ substituent to the electron pairs on the oxygen atom which is now the reaction centre. This effect will be particularly marked in (19b), where the anion will be stabilised substantially by delocalisation of its -ve charge, and the ionisation equilibrium for p -NO₂ phenol thereby displaced over towards the right in the anion's favour; thus increasing this phenol's strength as an acid.

The value for $\sigma_{p\text{-NO}_2}$ obtained from the standard reaction (18a \rightleftharpoons 18b) clearly does not take into account the heightened effect of this 'through-conjugation', which is why the point for p -NO₂—and for p -CN—is off the line in Fig. 13.4. Such through-conjugation can, however, be allowed for by using the aqueous ionisation of phenols to establish a set of new, alternative, σ values, for p -NO₂ and other comparable electron-withdrawing substituents: these new values may then be used for reactions in which through-conjugation can occur.

This can be achieved by first plotting $\log K_X/K_H$ against σ_X for m -substituted phenols only (which cannot be involved in through-conjugation), then the slope of the resulting straight line will give the value of ρ , the reaction constant, for this reaction. Using this value in the normal Hammett equation ([6], p. 363), enables us to calculate the new, revised, σ_{p^-} value for p -NO₂, and for similar substituents capable of through-conjugation. These revised figures are generally referred to as σ_{p^-} values, and a number are compared with the normal σ_{p^-} values below:

Substituent, X	σ_{p^-X}	σ_{p-X}
CO ₂ Et	0.68	0.45
COMe	0.84	0.50
CN	0.88	0.66
CHO	1.03	0.43
NO ₂	1.27	0.78

An exactly analogous situation will arise where there is the possibility of direct through-conjugation between a suitable electron-donating p -substituent and a reaction centre at which +ve charge is developing. A good example is solvolysis (S_N1) of the

tertiary halides, 2-aryl-2-chloropropanes (20), shown in Fig. 13.5:

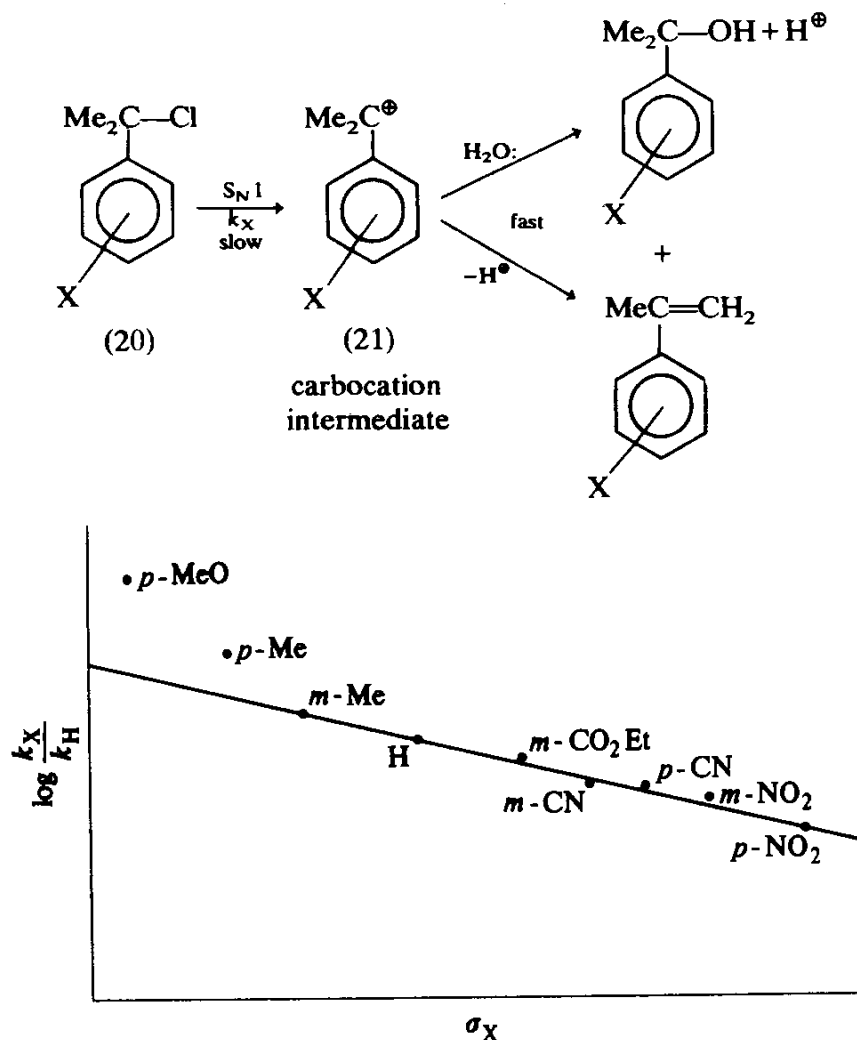
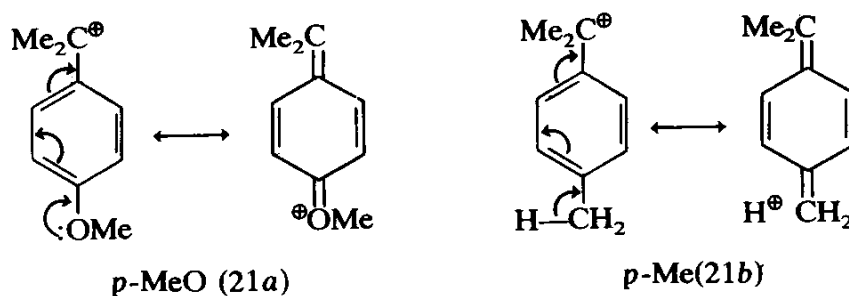


Fig. 13.5

Solvolysis of the $p\text{-MeO}$ and $p\text{-Me}$ chlorides is found to be faster ($p\text{-MeO} \approx 800$ times) than would have been predicted from their σ_p values. This stems from the stabilisation, by through-conjugation, of the carbocationic intermediates (21a and 21b) which are developing during the slow, rate-limiting step of the overall reaction:



The fact that development of +ve charge, in the transition state for

this slow step, is substantial is borne out by the large $-ve$ ρ value, -4.54 , for the reaction. By using this solvolysis as a new standard reaction, it is possible, as with σ_p^- , to obtain in an exactly analogous manner a set of σ_p^+ values that make allowance for through-conjugation by powerful electron-donating p -substituents; a number of these revised figures are compared with the corresponding σ_p -values below:

Substituent, X	σ_{p-X}^+	σ_{p-X}
C_6H_5	-0.18	-0.01
Me	-0.31	-0.17
MeO	-0.78	-0.27
NH_2	-1.30	-0.66
NMe_2	-1.70	-0.83

So for each p -substituent we now have available *two*, alternative, substituent constants— σ_{p-X}^- and σ_{p-X} for electron-withdrawing substituents or σ_{p-X}^+ and σ_{p-X} for electron-donating substituents—whose use depends on whether through-conjugation between p -substituent and reaction centre does, or does not, take place in a particular reaction. It would be nice to think that these dual substituent constant values would now take care of all eventualities, and an analysis was therefore made of no less than eighty different reactions to see whether use of σ_{p-X}^- or σ_{p-X} , and σ_{p-X}^+ or σ_{p-X} , would lead to straight line plots in all cases. In fact, it was found that the values required for, say, p - NO_2 did not cluster round *either* $0.78(\sigma)$ or $1.27(\sigma^-)$, but were spread more or less evenly throughout the range between these two, limiting values; and similarly for p -MeO, between $-0.27(\sigma)$ and $-0.78(\sigma^+)$.

On reflection, this is seen to be hardly surprising. The extent of the change in electron density at the reaction centre—an atom attached directly to the benzene ring in such reactions—during the slow, rate-limiting step will obviously differ from one reaction to another. So too, therefore, will the degree of response (*via* through-conjugation) elicited from the same p -substituent towards differing reactions. Hence the apparent need for a range of different σ_{p-X} values for a particular p -substituent, reflecting the differing degrees of through-conjugation elicited from it by different reactions.

13.3.7 Yukawa-Tsuno equation

There have been a number of attempts, by the introduction of a further parameter into the Hammett equation, to quantify this graded response—*via* through-conjugation—on the part of a p -substituent. Among the best known of these is the Yukawa-Tsuno equation, [7], which, in the form shown here, is

$$\log \frac{k_X}{k_H} = \rho[\sigma_X + r(\sigma_X^+ - \sigma_X)] \quad [7]$$

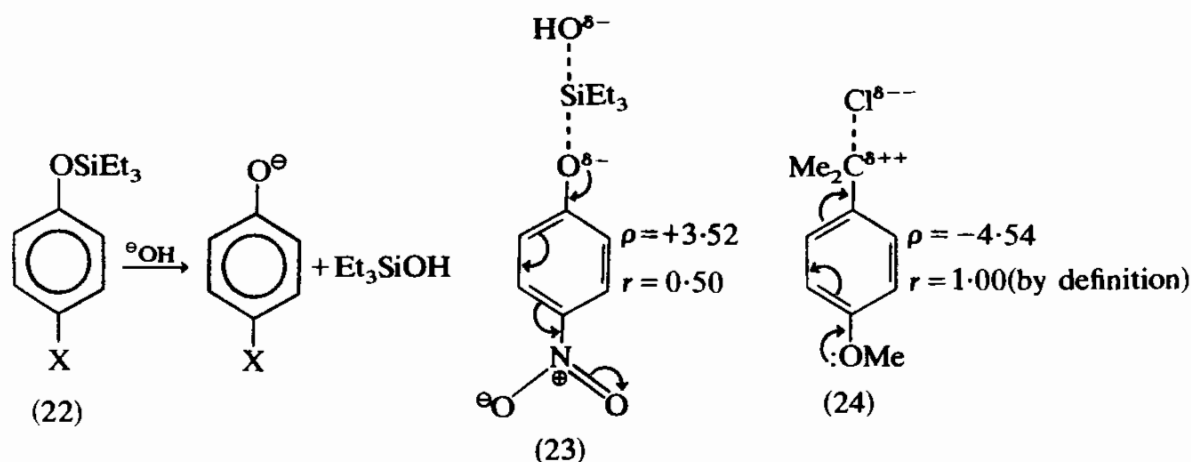
applicable to electron-donating *p*-substituents; for electron-withdrawing *p*-substituents σ_X^+ would, of course, be replaced by σ_X^- . The new parameter, *r*, intended as a measure of the through-conjugation operating in a particular reaction, is given the value of 1.00 for solvolysis of the tertiary halides, 2-aryl-2-chloropropanes (20). For this reaction [7] does, of course, then simplify to [8],

$$\log \frac{k_X}{k_H} = \rho \sigma_X^+ \quad [8]$$

which is reasonable enough as it was this reaction that we used (p. 371) to define σ_X^+ in the first place, for electron-donating *p*-substituents capable of considerable through-conjugation! Similarly, for a reaction in which no through-conjugation occurs *r* will be zero, and [7] will then, of course, simplify to the original, simple Hammett equation [6]:

$$\log \frac{k_X}{k_H} = \rho \sigma_X \quad [6]$$

To evaluate *r* for other reactions, we can obtain ρ for the reaction by measuring k_X values for *m*-substituted compounds only, and then measure k_X for *p*-substituted compounds where the values of σ_{p-X} and σ_{p-X}^+ , or σ_{p-X}^- , are already known. Using [7], *r* can then be evaluated by calculation, or by graphical methods. Thus for the base-catalysed hydrolysis of *p*-substituted phenoxytriethylsilanes



(22), the value of *r* is found to be 0.50. This extent of through-conjugation—by a substituent such as *p*-NO₂—suggests the development of substantial -ve charge ($\rho = +3.52$) in the transition state (23) for the rate-limiting step. This will not, however, be so far advanced as the development of +ve charge ($\rho = -4.54$) in the transition state (24) for the standard reaction, halide solvolysis, where $r = 1.00$. As, in each case, the development of charge in the transition state goes hand-in-hand with bond-breaking between the

reaction centre and the leaving group, the magnitude of r can perhaps be construed as some indication of the extent of such bond-breaking by the time the transition state has been reached.

It is, however, important to resist the temptation to introduce new parameters into the Hammett equation merely to achieve a better 'fit' with the experimental data. This is particularly true where, as in some cases, it may be difficult to ascribe real significance, in physical terms, to the new parameter anyway. It is in fact possible, as we shall see, to obtain much highly relevant information about reaction pathways using simple Hammett plots only.

13.4 USES OF HAMMETT PLOTS

Having now given some consideration to the significance that can be attached to σ_X and ρ in more familiar physical terms, it is possible to go on and discuss the actual uses that can be made of them in providing information about reactions and the pathways by which they take place.

13.4.1 Calculation of k and K values

The simplest possible use that can be made of the Hammett equation is to calculate k or K for a specific reaction of a specific compound, where this information is not available in the literature, or indeed where the actual compound has not even been prepared yet. Thus it is known that the base-catalysed hydrolysis of ethyl *m*-nitrobenzoate is 63.5 times as fast as the hydrolysis of the corresponding unsubstituted ester under parallel conditions; what then will be the comparable rate for base-catalysed hydrolysis of ethyl *p*-methoxybenzoate under the same conditions? Looking at the table of σ_X values (p. 363), we find that $\sigma_{m\text{-NO}_2} = 0.71$, while $\sigma_{p\text{-MeO}} = -0.27$. Then from the Hammett equation [6] (p. 363):

$$\textcircled{1} \quad \log \frac{k_{m\text{-NO}_2}}{k_H} = \rho \sigma_{m\text{-NO}_2} \quad [6a]$$

$$\text{i.e.} \quad \log \frac{63.5}{1} = \rho \times 0.71 \quad \therefore \rho = 2.54$$

$$\textcircled{2} \quad \log \frac{k_{p\text{-MeO}}}{k_H} = \rho \sigma_{p\text{-MeO}} \quad [6b]$$

$$\text{i.e.} \quad \log \frac{k_{p\text{-MeO}}}{k_H} = 2.54 \times -0.27 \quad \therefore \frac{k_{p\text{-MeO}}}{k_H} = 0.21$$

When $k_{p\text{-MeO}}$ subsequently came to be determined experimentally, $k_{p\text{-MeO}}/k_H$ was indeed found to be 0.21, so the calculated value was pretty satisfactory! In fact, σ_X and ρ values are rarely used for such a purpose, they are employed much more often in providing salient data about reaction pathways.

13.4.2 Deviations from straight line plots

We have already seen (p. 368) how the sign and magnitude of ρ , the reaction constant, can provide useful information about the development (or dissipation) of charge (+ve or -ve) on going from starting materials to the transition state for the rate-limiting step of a reaction. We have also seen (p. 369) how deviations from straight line plots using normal σ_x , substituent constant, values led to the definition of σ_x^+ or σ_x^- values to take into account through-conjugation between certain *p*-substituents and the reaction centre. The need to use other than the normal σ_x values indicates the occurrence of such through-conjugation in a particular reaction, and the Yukawa-Tsuno parameter, r , then provides a measure of its extent.

Paradoxically, Hammett plots are usually most informative at the very point at which they depart from linearity, but the major inference that can be drawn from this departure is found to differ depending on whether the deviation is concave 'upwards' or concave 'downwards'.

13.4.3 Concave upwards deviations

13.4.3.1 Acetolysis of 3-aryl-2-butyl brosylates

An interesting case in point is the acetolysis of 3-aryl-2-butyl *p*-bromobenzenesulphonates or brosylates (25), for which the Hammett plot is shown in Fig. 13.6. The lower right-hand side of the

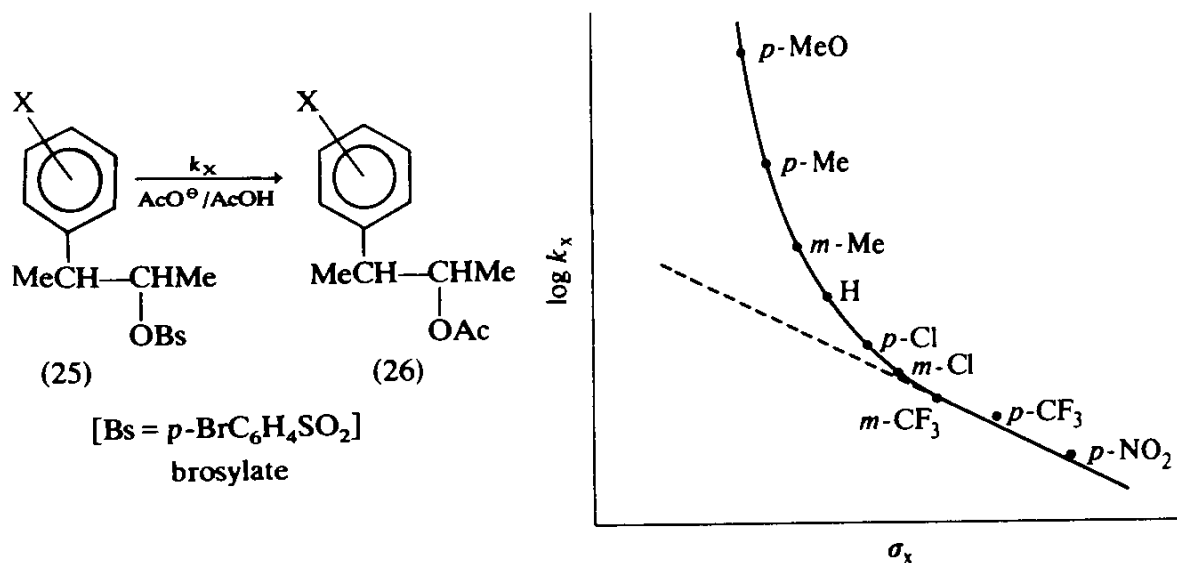
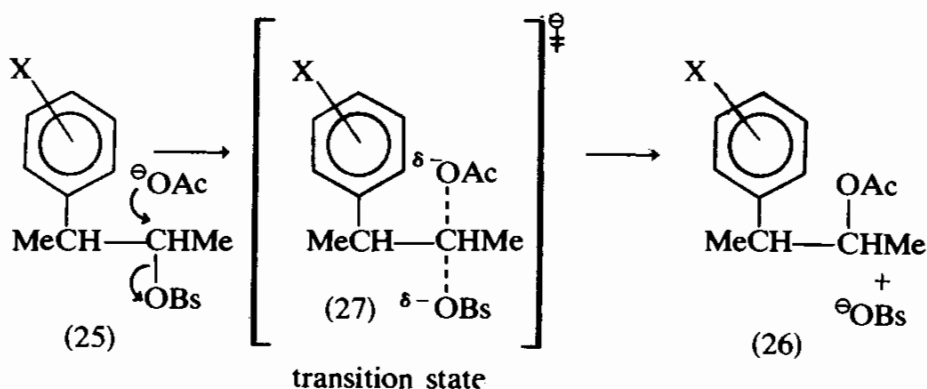


Fig. 13.6

plot—where the substituents are powerfully electron-withdrawing—is a straight line whose slope indicates a ρ value for the reaction of -1.46 . On moving across to the left—as the substituents become less electron-withdrawing—the plot now curves upwards, indicating that the rate of acetolysis of these species is *faster* than we would have expected it to be on the basis of the σ_X values for their substituents.

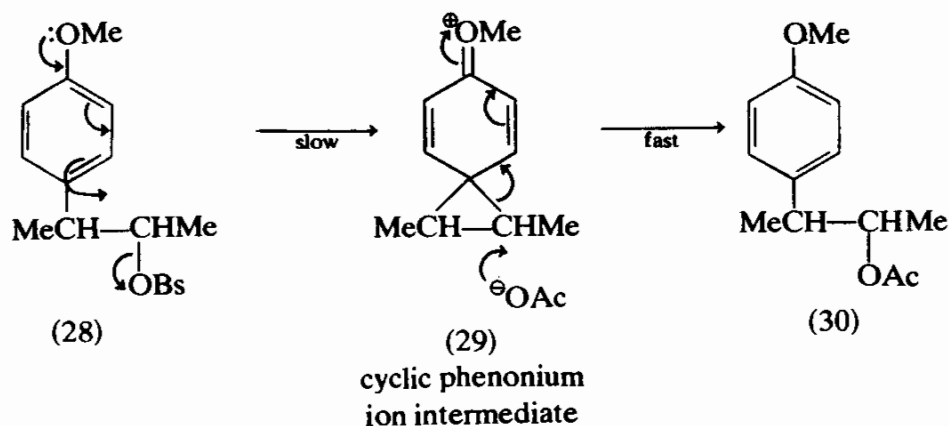
What we might expect as a pathway for this reaction would be simple S_N2 displacement (p. 98) of the good leaving group—brosylate anion—by acetate anion:



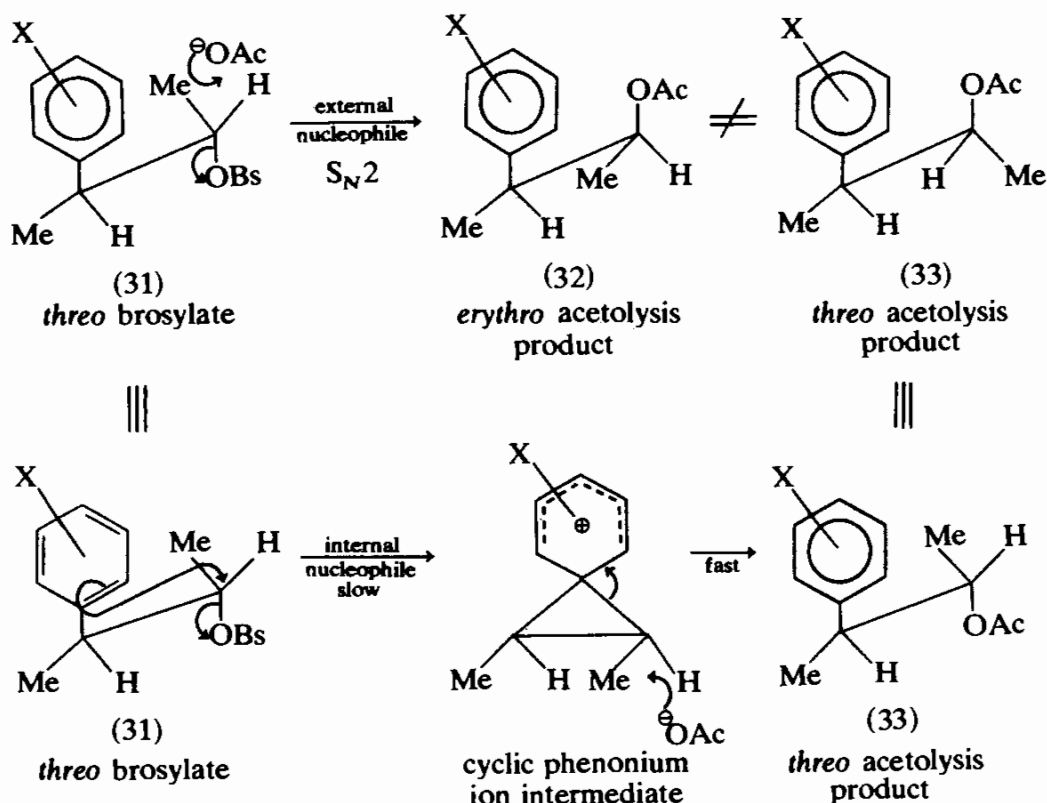
The smallish $-ve$ ρ value (-1.46) is compatible with such a pathway, given that in the transition state (27) breaking of the $\text{C}-\text{OBs}$ bond, is somewhat more fully advanced than formation of the $\text{AcO}-\text{C}$ bond, resulting in the transient development of a small amount of $+ve$ charge at the reaction centre. This is in no sense unreasonable with (a) a secondary carbon atom as reaction centre (*cf.* p. 82), and (b) so good a leaving group (*cf.* p. 98); this pathway would be increasingly aided, albeit weakly, as the substituent X becomes less electron-withdrawing, i.e. the rate of acetolysis might be expected to increase, gradually and linearly, from right to left across the plot in Fig. 13.6.

To account for the departure from linearity, as X becomes more electron-donating, it would seem that the substituted benzene ring must gradually become capable of exerting some more direct effect on the reaction centre in (25) than it does in the S_N2 pathway. It is significant in this respect that increasing electron-donation by X will increase the nucleophilicity of the substituted benzene ring itself, thereby enabling it to function—in competition with $\ominus\text{OAc}$ —as a neighbouring group (p. 93) or ‘internal’ nucleophile, e.g. when $X = \text{MeO}$ (28). This alternative reaction pathway would then involve slow, rate-limiting formation of the cyclic phenonium ion intermediate (29, *cf.* p. 105), followed by its rapid ring-opening by $\ominus\text{OAc}$

to yield the normal acetolysis product (30):



Support for the suggestion that Fig. 13.6 involves a change in actual reaction pathway is provided by acetolysis of the *threo* diastereoisomer (31) of the brosylate. Acetolysis leads to two different distinguishable, diastereoisomers whose relative proportion will depend on how much of the total reaction proceeds by *external* nucleophilic attack *via* the S_N2 pathway (*erythro* product, 32), and how much by *internal* nucleophilic attack *via* a cyclic phenonium ion intermediate (*threo* product, 33):



The two, alternative, acetolysis products (32 and 33), being diastereoisomers not mirror images, may then be separated, or their

relative yields estimated by spectroscopic methods. It is found that the yield of *threo* product (33) varies considerably as the nature of X, the substituent in the benzene ring, is changed:

Substituent, X	Yield of <i>threo</i> product* (33)	
<i>p</i> -MeO	100	
<i>p</i> -Me	88	
<i>m</i> -Me	68	
H	59	* = percentage of reaction
<i>p</i> -Cl	39	proceeding <i>via</i>
<i>m</i> -Cl	12	internal
<i>m</i> -CF ₃	6	nucleophilic
<i>p</i> -NO ₂	1	attack

When X = *p*-MeO, the most electron-donating substituent at the top left-hand corner of Fig. 13.6, 100% of acetolysis is proceeding *via* internal nucleophilic attack by *p*-MeOC₆H₄; when X = *m*-Cl, just coming on to the straight line part of the plot in Fig. 13.6, only 12% of the total reaction is proceeding *via* the internal route; while when X = *p*-NO₂, the most electron-withdrawing substituent, only 1% of the total reaction is now proceeding by this route.

When a simple Hammett plot exhibits an upward deviation, i.e. is concave upwards as in Fig. 13.6, then this can usually be taken as evidence of a change in overall reaction pathway, as the nature of the substituent is varied. That a change in reaction pathway should lead to an *upward* deviation is reasonable enough: in Fig. 13.6, there is, at the point where departure from linearity occurs, nothing to prevent the initial S_N2 pathway from continuing to operate (along the dotted extrapolation). Any change to a new pathway must offer a less demanding, and hence *faster* (necessarily upward-curving), alternative or, of course, the initial pathway would continue to prevail and no departure from the original straight line would then be observed.

13.4.3.2 Hydrolysis of ArCO₂R in 99.9% H₂SO₄

Sometimes departure from the straight line is considerably more abrupt than in Fig. 13.6; a particularly good example is the hydrolysis, in 99.9% H₂SO₄, of the substituted methyl (34*a*), and ethyl (34*b*), benzoates shown in Fig. 13.7 (p. 379).

Considering first the simpler of the two cases, the straight line for the methyl esters (34*a*) which has a ρ value of -3.25 . From this ρ value it is apparent that this reaction cannot be proceeding *via* the normal (A_{AC}2) pathway (p. 241) for acid-catalysed ester hydrolysis which, as we know (reaction 6, p. 364), has a ρ value of $+0.03$. That value refers, however, to hydrolysis being carried out with dilute sulphuric acid, while here 99.9% sulphuric acid is being used: one

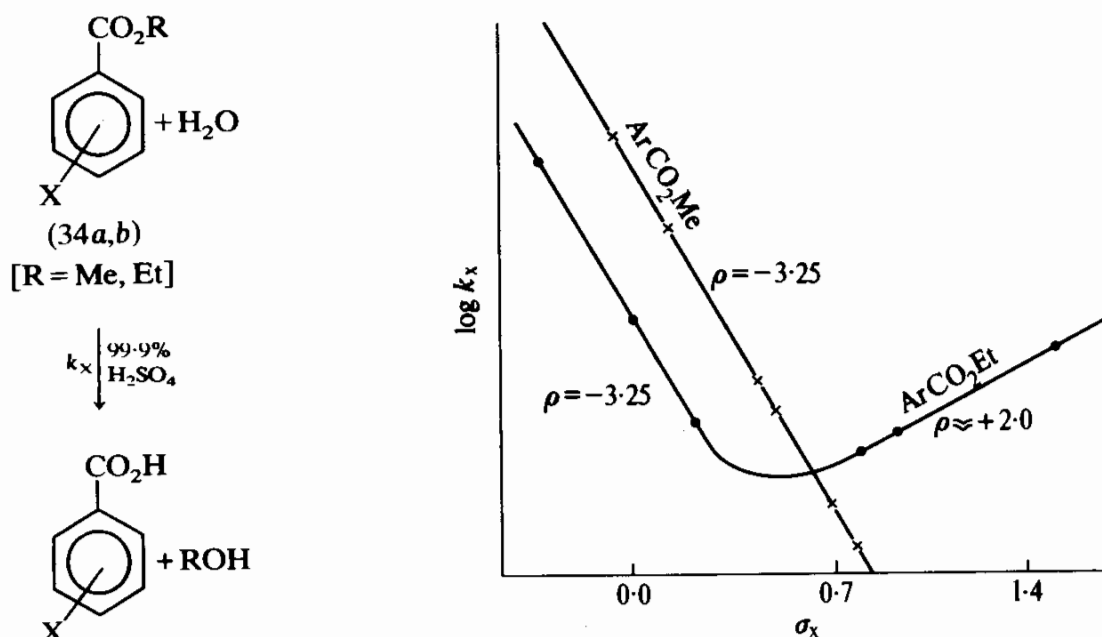
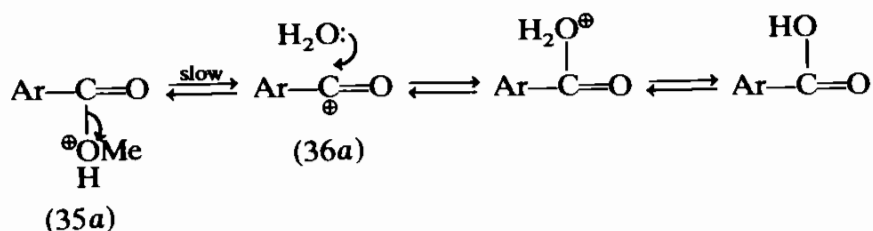


Fig. 13.7

result of which is to make the concentration of water available for hydrolysis very low.

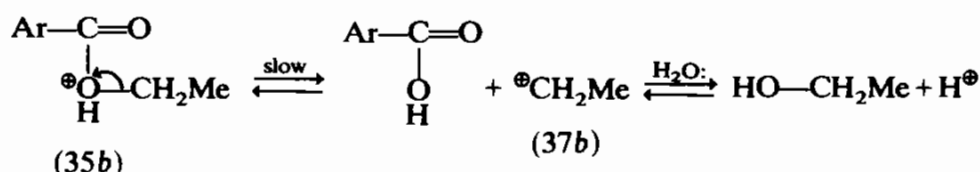
We have, however, already seen an alternative acid hydrolysis pathway ($A_{AC}1$, p. 242) in which a water molecule is not involved in the slow, rate-limiting step. In addition, this step is one in which considerable +ve charge is developed at the reaction centre as the protonated ester (35a) is converted into the acyl cation intermediate (36a): a necessary requirement for a reaction with a large -ve (-3.25) ρ value:



The same $A_{AC}1$ pathway must also be operating initially for the ethyl esters (34b), on the left-hand side of Fig. 13.7, as the ρ value (-3.25) for this reaction is the same as that for the methyl esters (34a). As the substituent in the benzene ring becomes more strongly electron-withdrawing, however, a sharp change in curvature is observed with the ethyl esters to a new straight line with a ρ value of $+2.0$. This now +ve ρ value requires a slow, rate-limiting step for hydrolysis in which +ve charge is decreased at the reaction centre—the overall reaction being increasingly accelerated as the substituent in the ring becomes more electron-withdrawing.

There is indeed yet another pathway for acid-catalysed ester

hydrolysis ($A_{AL} 1$, p. 241) that would fulfil this requirement:



Loss of MeCH_2^+ the ethyl cation (37b), leads to a marked decrease in +ve charge adjacent to the reaction centre (had it actually been from the reaction centre itself the +ve value of ρ would have been much larger); this carbocationic intermediate (37b) will then react rapidly with any available water to yield ethanol.

The question does then arise, given the observed shift in reaction pathway for the ethyl esters (34b), why does a similar shift not occur with the corresponding methyl esters (34a)? Such a shift would, of course, necessitate the formation of a methyl, CH_3^+ , rather than an ethyl, MeCH_2^+ (37b), cation in the slow, rate-limiting step. CH_3^+ is known to be considerably more difficult to form than is MeCH_2^+ and this difference is apparently great enough to rule out, on energetic grounds, such an $A_{AC}1 \rightarrow A_{AL}1$ shift with the methyl esters, despite potential assistance (to $A_{AL}1$) from increasingly electron-withdrawing substituents.

13.4.4 Concave downwards deviations

There are, however, also examples of deviations from simple Hammett plots in which the curvature is in the opposite direction, concave downwards, and these deviations have a rather different significance.

13.4.4.1 Cyclodehydration of 2-phenyltriarylmethanols

A good example is the cyclodehydration of some substituted 2-phenyltriarylmethanols (38), in 80% aqueous ethanoic acid containing 4% H_2SO_4 at 25° , to yield the corresponding tetraarylmethanes (39), as shown in Fig. 13.8 (p. 381).

Two of the benzene rings in (38) each carry a *p*-substituent (X and Z, respectively), and the value of σ actually plotted is $\Sigma\sigma$: the sum of the σ values for X and Z. The plot in Fig. 13.8—of $\log k_{\text{obs}}$ for the reaction against $\Sigma\sigma$ —is clearly a composite of two straight lines, one on the left with $\rho = +2.67$, and one on the right with $\rho = -2.51$.

There seems little doubt that the overall reaction follows a four-step pathway, the first two steps constituting an E1 (p. 247) elimination of water to yield a carbocationic intermediate (40), which then, in the last two steps, effects internal electrophilic

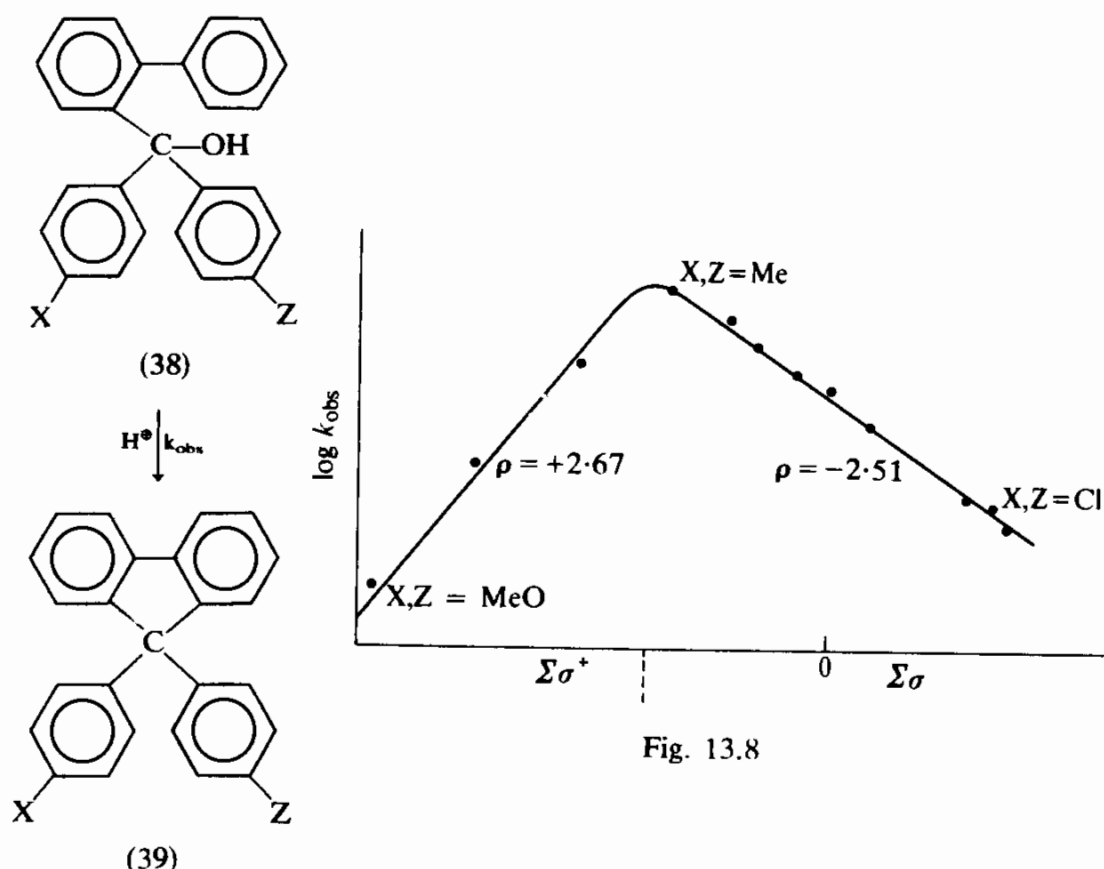
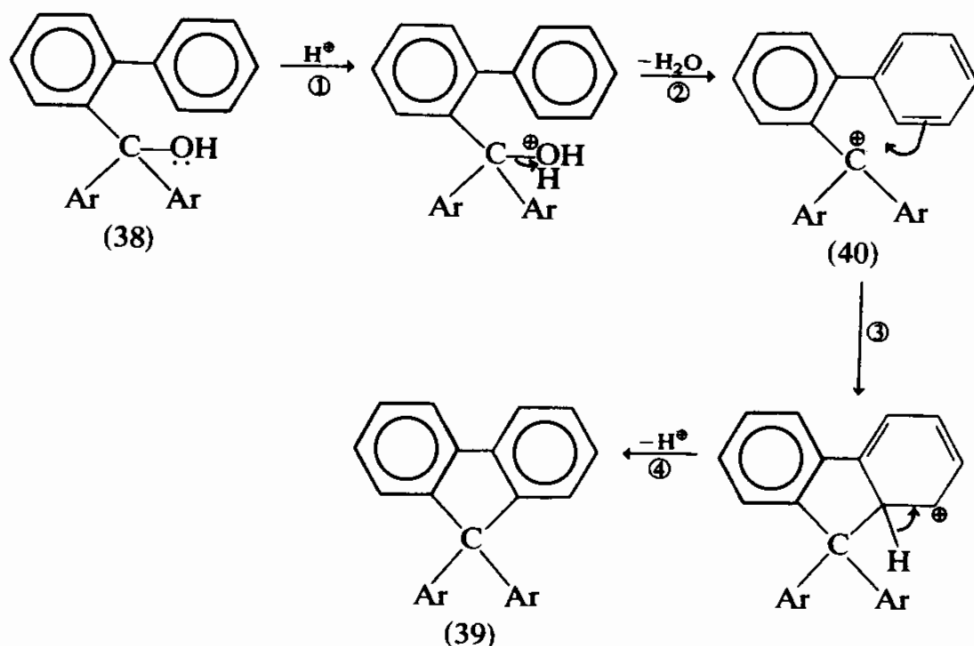


Fig. 13.8

substitution on the 2-phenyl nucleus to yield the product tetraaryl-methane (39):

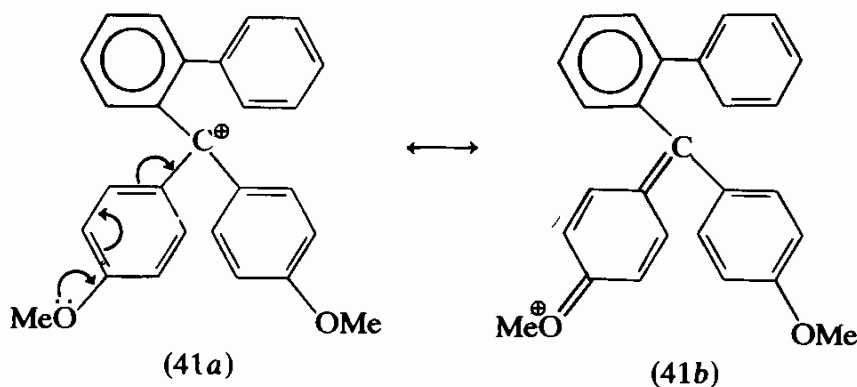


The question then arises—which step in the overall reaction is likely to be the slow, and hence rate-limiting, one? It's unlikely to be

step ①: initial protonation in acid-catalysed dehydration is generally rapid; or step ④: final loss of proton in aromatic electrophilic substitution is also generally rapid. This leaves steps ② and ③ as possible candidates for the slow step overall, and fortunately a clear distinction can be made between them. In step ②, +ve charge is *increasing* at the reaction centre (the carbon atom carrying the two substituted Ar groups), while in step ③, +ve charge is *decreasing* at the reaction centre. How does this match up with the requirements of Fig. 13.8 (p. 381)?

The right-hand side of the plot in Fig. 13.8 has a -ve ρ value (-2.51) indicating the development of substantial +ve charge at the reaction centre during the overall, rate-limiting step. This would, of course, be compatible with step ② being rate-limiting, but not with step ③. For the left-hand side of the plot in Fig. 13.8, exactly the reverse is true; here a +ve ρ value (+2.67) indicates a substantial decrease of +ve charge at the reaction centre, which would be compatible with step ③ being rate-limiting, but not with step ②.

It is significant that the substituents involved at the far left-hand side of the plot (38; X, Z = MeO) are powerfully electron-donating, and thus capable of stabilising the carbocation (41a \leftrightarrow 41b), developing in step ②, by delocalisation of its +ve charge. It is indeed



found that the $\log k_{\text{obs}}$ values on the left-hand side of Fig. 13.8 give a better straight line when plotted against $\Sigma\sigma^+$, rather than against $\Sigma\sigma$, because of the through-conjugation (41a \leftrightarrow 41b) between these *p*-substituents and the reaction centre.

In (38; X, Z = MeO) this conjugative stabilisation results in easy formation of the carbocation (41), i.e. to a rapid step ②; but the consequent delocalisation of +ve charge, away from the reaction centre (41a \leftrightarrow 41b), clearly makes (41) a less effective electrophile, i.e. step ③—electrophile attack on the benzene nucleus—is therefore slow. It is thus step ③ that is slow, and hence rate-limiting overall, for compound (38; X, Z = MeO). On moving across Fig. 13.8, from left to right, the substituents become less electron-donating, delocalisation of +ve charge thereby becomes less pronounced, and the reaction centre progressively more electrophilic.

Rate-limiting step ③ is thus speeded-up, and the overall reaction rate therefore increases, i.e. the slope of the plot is upwards from left to right (ρ is +ve). Also on moving from left to right, decreasing through-conjugation, as the substituents become less electron-donating, makes carbocation formation more difficult; thus step ② is being slowed down as step ③ is being speeded-up. There must, therefore, come a point at which speeding-up step ③ catches up with the slowing-down step ②; any further decrease in electron-donation by the substituents must result in step ② becoming slower than step ③, thereby making it now rate-limiting for the overall reaction. This shift in rate-limiting step from step ③ \rightarrow step ② occurs, in Fig. 13.8, with the compound (38; X, Z = Me).

Still further decrease in electron-donation by the substituents, beyond this point, will result in still further slowing-down of step ②—now the rate-limiting step—and hence slowing-down of the overall reaction, i.e. the slope on the right-hand side of the plot is now downwards from left to right (ρ is -ve). For a reaction in which such a shift of rate-limiting step is observed (as the electron-donating/-withdrawing ability of the substituent is changed) there will be one substituent, or narrow range of substituents, for which the balance between the rates of step ② and step ③ is such as to make the overall reaction rate a maximum.

This happens in Fig. 13.8, as we have seen, with the compound (38; X, Z = Me). On each side of this maximum the, different, rate-limiting step will be slowing down progressively, and so therefore will the overall reaction rate. Shifts in rate-limiting step, within the same overall reaction pathway, are thus distinguished by concave *downwards* deviations in Hammett plots; this in contrast to the concave *upwards* deviations which, as we have already seen (p. 364), are characteristic of a change in overall reaction pathway.

13.5 STERIC EFFECTS

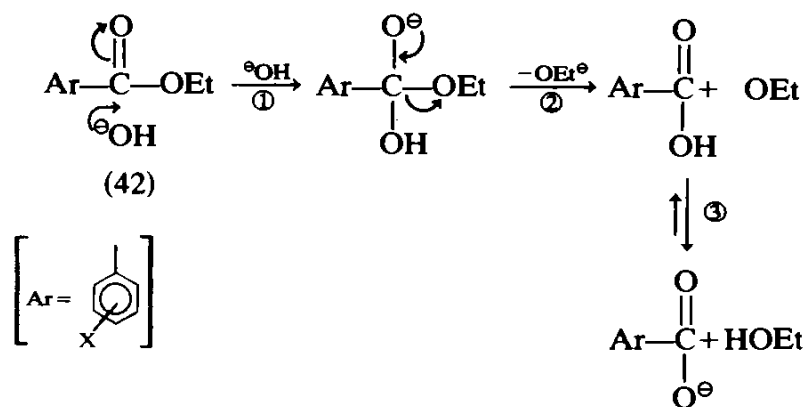
Quite early on (p. 361) in this discussion of linear free energy relationships consideration was restricted to the side-chain reactions of *m*- and *p*-substituted benzene derivatives. The reactions of *o*-substituted benzene derivatives, and indeed of aliphatic compounds, were excluded because of the operation of steric and other effects, which led to non-linear, or even to apparently random, plots.

The success and utility of Hammett plots, and the realisation that they are often of most value diagnostically when they do indeed diverge from linearity, has emboldened a number of workers to seek, with suitable modifications, to extend their scope to a much wider range of compounds. The most general and successful of these extensions was proposed by Taft.

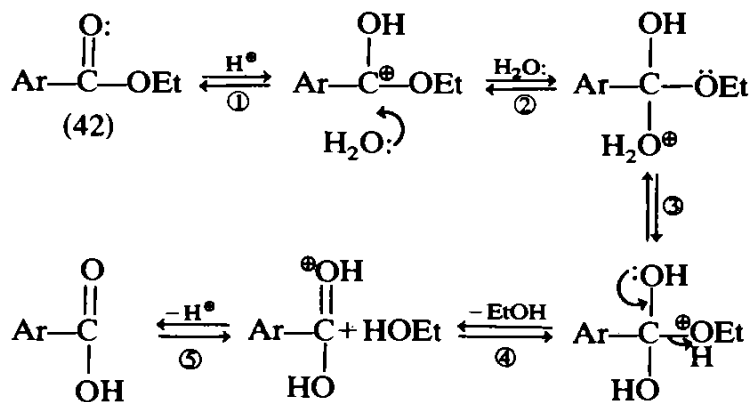
13.5.1 Taft equation

Acting on a suggestion originally made by Ingold, Taft began by comparing the relative susceptibility to polar substituent effects (the ρ value) of the hydrolysis—under acid-catalysed ($A_{AC}2$, p. 241) and under base-catalysed ($B_{AC}2$, p. 239) conditions—of *m*- and *p*-substituted benzoate esters (42).

The ρ value for base-catalysed hydrolysis (+2.51) is +ve and quite large, reflecting the development of not inconsiderable -ve charge at the reaction centre in the rate-limiting step—attack on this centre by $^{\ominus}\text{OH}$ (step ① in the $B_{AC}2$ pathway). By contrast, the ρ value for acid-catalysed hydrolysis (+0.03) is very nearly zero; which means, of course, that the rate of this hydrolysis does not vary significantly from one ester to another, no matter what the *m*- or



Base-catalysed hydrolysis ($B_{AC}2$): $\rho = 2.51$

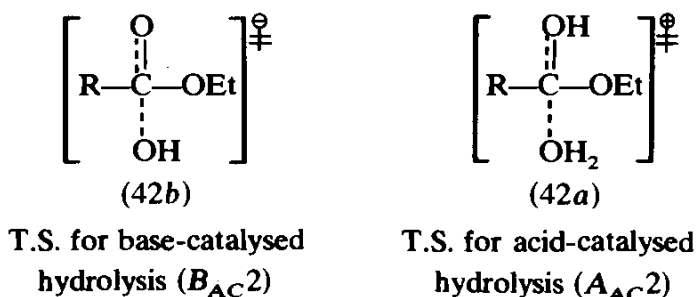


Acid-catalysed hydrolysis ($A_{AC}2$): $\rho = 0.03$

p-substituent present. The ρ value for this hydrolysis is so small, despite their being considerable redistribution of +ve charge in the slow step (step ②), because the overall rate of reaction, i.e. k_{obs} (which is plotted to evaluate ρ), is determined not solely by k_2 for this slow step, but involves also K_1 for the preceding, reversible, step ①. These two terms all but cancel each other out, in so far as susceptibility of the two steps to electron-donation/-withdrawal by

polar substituents is concerned, and the overall ρ value for the reaction is thus virtually zero.

If we now extend our consideration of base-catalysed ($B_{AC}2$), and acid-catalysed ($A_{AC}2$), hydrolysis to esters in general, including aliphatic ones (RCO_2Et), we see that there is a close similarity between the transition states (42*b* or 42*a*) for the rate-limiting step in each of the two pathways: they are both tetrahedral; and differ



only in the second of them having two protons more than the first. Protons, being very small, exert comparatively little steric influence; it is therefore a not unreasonable assumption that any steric effect stemming from the group R is, because of the close spatial similarity of the two transition states, substantially the same in both acid- and base-catalysed hydrolysis.[†] It then becomes possible to write a Hammett type equation, [9], to represent the operation of the *polar* effect only of substituent R in ester hydrolysis:

$$\log \left[\frac{k_R}{k_0} \right]_{\text{base}} - \log \left[\frac{k_R}{k_0} \right]_{\text{acid}} = \rho^* \sigma_R^* \quad [9]$$

As the steric effect exerted by R is essentially the same in both modes of hydrolysis, the two steric terms will cancel each other out, and will thus not appear in equation [9].

Taft then gave ρ^* in [9], the value 2.48, derived by subtracting the ρ value for acid-catalysed hydrolysis of benzoate esters (0.03) from the ρ value for base-catalysed hydrolysis of the same esters (2.51). He took as his reference substituent $R = \text{Me}$, rather than $R = \text{H}$, so that k_0 in [9] refers to MeCO_2Et rather than HCO_2Et . Then by kinetic measurements on the acid- and base-catalysed hydrolysis of a series of esters containing R groups other than Me, it is possible—using [9]—to evaluate σ_R^* for each of these different R groups with respect to Me, for which by definition $\sigma_{\text{Me}}^* = 0$ (cf. H with $\sigma_{\text{H}} = 0$ for benzoic acid ionisation, p. 363). By giving ρ^* here the value 2.48, the resulting σ_R^* values—which are a measure of the polar effect only exerted by R—do not differ too greatly in mag-

[†] Such an assumption does, however, neglect the possibility that the degree of solvation of +vely and -vely charged T.S.s could be markedly different, thereby greatly influencing the relative rates of the two hydrolyses.

nitude from the values of σ_X , σ_X^+ and σ_X^- with which we are already familiar (p. 363).

Then, employing the more general equation [10], it is possible to use these σ_R^* values, in conjunction with suitable kinetic measurements of k_R and k_{Me} , to evaluate ρ^* for other

$$\log \frac{k_R}{k_{Me}} = \rho^* \sigma_R^* \quad [10]$$

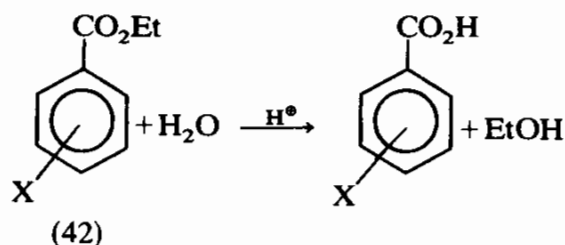
reactions of a whole range of aliphatic compounds in addition to esters. Using [10] in this way, straight line plots were obtained for a number of different reactions of aliphatic compounds.

13.5.2 Steric parameters, E_s and δ

After all the emphasis we placed earlier (p. 361) on steric effects, obtaining a straight line plot may at first sight seem a rather surprising result; especially, given that the relation [10] takes into account only the *polar* effect exerted by R. However, obtaining a straight line plot, using [10], does not necessarily mean that *no* steric effects are operating in a reaction. It means only that there is no substantial *change* in the operation of such effects on going from starting materials to the transition state for the rate-limiting step of the overall reaction (or on going from starting materials to products for an equilibrium).

It is not necessary to look very far to find aliphatic reactions that do *not* yield straight line plots with [10], however; and, as with previous deviations from linearity (p. 375), these departures are commonly much more informative about the details of reaction pathways than are neat straight lines. Where such departures from linear (polar effects only) plots are observed, suggesting the operation of significant—and changing—steric effects, it is possible to incorporate a *steric substituent parameter*, E_s , whose evaluation is based on an earlier observation.

Thus we have already seen (p. 384) that the acid-catalysed hydrolysis of *m*- and *p*-substituted benzoate esters (42) is (with a ρ value of 0.03) essentially uninfluenced by any polar effect exerted by the substituent, X; and this substituent is sufficiently far removed from the reaction centre to be clearly incapable of exerting any



steric effect on it either. These esters thus all undergo acid-catalysed

hydrolysis at essentially the same rate. There is no reason to believe that acid-catalysed hydrolysis of aliphatic esters, RCO_2Et , will be any more susceptible to polar effects than was the corresponding hydrolysis of benzoate esters. If then different hydrolysis rates *are* observed with aliphatic esters as R is varied, these must reflect differing steric effects exerted by the different R groups. Such aliphatic esters are indeed found to undergo hydrolysis at markedly different rates, so it is possible, taking Me as the standard substituent once again, to use equation [11]

$$\log \left[\frac{k_{\text{RCO}_2\text{Et}}}{k_{\text{MeCO}_2\text{Et}}} \right]_{\text{acid}} = E_s \quad [11]$$

to evaluate E_s , the steric substituent parameter, for R . E_s values, obtained in this way for a number of different substituents, are listed below:

R in RCO_2Et	E_s	R in RCO_2Et	E_s
H	+1.24	$\text{Me}(\text{CH}_2)_3$	-0.39
Me	0 (by definition)	Me_2CHCH_2	-1.13
Et	-0.07	Me_3C	-1.54
ClCH_2	-0.24	Me_3CCH_2	-1.74
ICH_2	-0.37	Ph_2CH	-1.76
PhCH_2	-0.38	Et_3C	-3.81

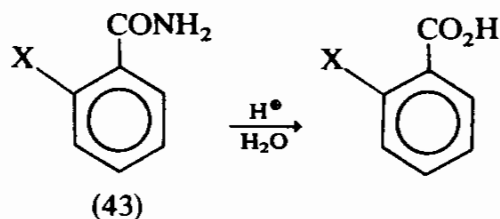
From the form of equation [11], the E_s value for Me , the reference substituent, will of course be 0. All substituents other than H have -ve E_s values because all substituents other than H are larger than Me , and the rate of hydrolysis of any ester RCO_2Et ($\text{R} \neq \text{H}$) will thus be slower than that of MeCO_2Et , in a reaction whose rate is governed solely by the steric effect of R .

It is found in practice that the value of the steric parameter, E_s , for a particular group, R , differs to some extent from one reaction to another. This is not altogether surprising as both the local environment of R and the size of the attacking reagent will vary from one reaction to another. It means, however, that on incorporating E_s into the Hammett type equation, [12], it is necessary to introduce a yet further parameter, δ , as a measure of a particular reaction's

$$\log \frac{k_{\text{R}}}{k_{\text{Me}}} = \rho^* \sigma_{\text{R}}^* + \delta E_s \quad [12]$$

susceptibility towards steric effects. In that sense δ is the steric parallel to ρ^* —which measures the reaction's susceptibility towards polar effects. The δ parameter is given the value 1.00 for acid-catalysed ester hydrolysis, as the standard reaction, and its value for other reactions can then be determined experimentally in the usual way.

Now that steric parameters have been introduced in this way, the treatment can be extended to include the reactions of *o*-substituted benzene derivatives as well. Thus for the acid-catalysed hydrolysis of *o*-substituted benzamides (43), the value of δ is found to be 0.81; so this reaction is apparently slightly less susceptible to the steric



effect of substituents than is the standard reaction, the acid-catalysed hydrolysis of *o*-substituted esters. In general, attempts to quantify *o*-substituent effects have not, however, been very successful. We are here, once again, faced with some dilemma as we were with the Yukawa-Tsuno equation (p. 374): how far does any additional information gained merit the very considerable effort involved in the experimental evaluation of such further parameters in the first place?

13.6 SOLVENT EFFECTS

One of the things our discussion of linear free energy relationship has not yet made any endeavour to take into account is the role played in reactions by the solvent. This despite the fact that the very great majority of organic reactions do take place in solution, with the solvent often playing a crucial role.

13.6.1 Change of ρ with solvent

It is, of course, true that some implicit consideration is given to the solvent in that the ρ value for a particular reaction is found to change when the solvent in which the reaction is carried out is changed:

Reaction	ρ
$\text{ArCO}_2\text{H}(44) + \text{H}_2\text{O} \rightleftharpoons \text{ArCO}_2^- (45) + \text{H}_3\text{O}^+ (\text{H}_2\text{O})$	1.00 (by definition)
" + " \rightleftharpoons " + " (50% aq. EtOH)	1.60
" + " \rightleftharpoons " + " (EtOH)	1.96
$\text{ArCO}_2\text{Et} + {}^\ominus\text{OH} \rightarrow \text{ArCO}_2^- + \text{EtOH}$ (70% aq. dioxan)	1.83
" + " \rightarrow " + " (85% aq. EtOH)	2.54

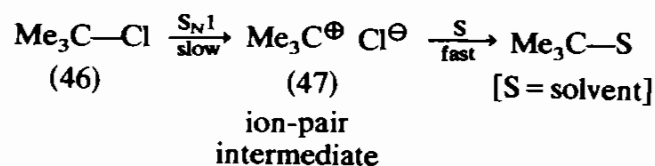
For ionisation of *m*- and *p*-substituted benzoic acids (44), the hydroxylic solvent is capable of solvating both the undissociated acid (44) and the carboxylate anion (45) obtained from its ionisation.

The relative effectiveness of such solvation—of negatively charged anion (45) with respect to neutral, undissociated acid (44)—is a major factor in determining the position of equilibrium, i.e. K_X . As the solvent is changed from water, with a dielectric constant of 79, to ethanol, with a dielectric constant of only 24, there will be a marked decrease in advantageous solvation of the charged anion (45) with respect to the uncharged acid (44). The relative importance of the polar effect exerted by electron-withdrawing substituents, in overall stabilisation of the carboxylate anion (i.e. in acid-strengthening: increasing K_X), will therefore *increase* as the dielectric constant of the solvent *decreases*. The value of ρ , the susceptibility of the reaction to the polar effect of a substituent, will also increase, therefore, on changing the solvent from water to ethanol.

13.6.2 Grunwald–Winstein equation

Attempts to correlate the differing rate of a particular reaction, when carried out in a range of different solvents, with the dielectric constant values for these solvents have not proved very rewarding. Attempts have therefore been made to establish empirical reactivity/solvent correlations along general Hammett lines. Among the more significant of these attempts has been that of Grunwald and Winstein on the solvolysis of halides. They sought to establish a solvent parameter, designated Y , which would correlate with the different rate constants found for solvolysis of the same halide in a range of different solvents.

They took as their standard reaction the S_N1 solvolysis of the tertiary halide, 2-chloro-2-methylpropane (46), and selected as their standard solvent 80% aqueous ethanol (80% EtOH/20% H₂O):



It is then possible to set up the Hammett-like relation, [13],

$$\log k_A - \log k_0 = Y_A - Y_0 \quad [13]$$

in which the rate constants, k_A and k_0 , refer to solvolysis of the tertiary halide (46) in a solvent A and in the standard solvent (80% aq. EtOH), respectively; while Y_A and Y_0 are the empirical solvent parameters for solvent A and for this standard solvent. By setting the value of Y_0 at zero and measuring k_A for the solvolysis of (46) in a range of different solvents, it is then possible, using [13], to derive

a Y_A value for each of them:

Solvent, A	Y_A	ϵ
H ₂ O	+3.49	78.5
aq. MeOH (50% H ₂ O)	+1.97	—
HCONH ₂	+0.60	109.5
aq. EtOH (30% H ₂ O)	+0.59	—
aq. EtOH (20% H ₂ O)	0 (by definition)	—
aq. Me ₂ CQ (20% H ₂ O)	-0.67	—
MeOH	-1.09	32.7
MeCO ₂ H	-1.64	6.2
EtOH	-2.03	24.3
Me ₂ CHOH	-2.73	18.3
Me ₃ COH	-3.26	12.2

These Y_A values are found not to run in parallel with the dielectric constant values for the solvents concerned. Obviously the dielectric constant value for the solvent must be involved in some way in Y_A , as separation of opposite charges is a crucial feature of the rate-limiting step in an S_N1 reaction: formation of the T.S. leading to the ion-pair intermediate (47). But specific solvation of the separating charges must also be involved and Y_A will reflect those, and quite possibly other properties of the solvent as well. It is common to describe Y_A as representing a measure of the 'ionising power' of the solvent A.

It is now possible to go a stage further, and write a not unfamiliar relation, [14], that now covers the solvolysis of halides in general, and not merely that of the

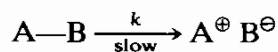
$$\log \frac{k_A}{k_0} = m Y_A \quad [14]$$

standard halide, 2-chloro-2-methylpropane (46). Here k_A and k_0 are the rate constants for solvolysis of any halide, in solvent A and in the standard solvent, respectively. Y_A has already been defined as a *solvent* parameter representing the ionising power of solvent A, while m is a *compound* parameter characteristic of the particular halide: it is given the value 1.00 for the standard halide, 2-chloro-2-methylpropane (46). The actual value of m can be taken as a measure of the susceptibility of the solvolysis of a particular halide towards the ionising power, Y_A , of that solvent:

Halide	m
PhCH(Me)Br(48)	1.20
Me ₃ CCl(46)	1.00 (by definition)
Me ₃ CBr	0.94
EtMe ₂ CBr	0.90
CH ₂ =CHCH(Me)Cl	0.89
EtBr(49)	0.34
Me(CH ₂) ₃ Br(50)	0.33

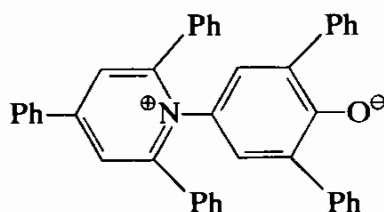
An alternative interpretation of m is that it provides some measure of the extent of ion-pair formation in the transition state for the rate-limiting step of the overall solvolysis reaction: it can then be put to some diagnostic use. Thus, ion-pair formation is known to be well advanced in the transition state for S_N1 solvolysis of 2-chloro-2-methylpropane (46), the standard halide, for which $m = 1.00$. Not altogether surprisingly the value of m for 1-bromo-1-phenylethane (48), in which the developing benzyl type cation, $[\text{PhCHMe}]^{\oplus}$, is stabilised by delocalisation of its +ve charge over the π -system of the attached benzene nucleus (cf. p. 84), is even larger—at 1.20. By contrast, the m values for the primary halides, bromoethane (49) and 1-bromobutane (50), are much lower—0.34 and 0.33, respectively. These values, indicating low susceptibility towards the ionising power of the solvent, are characteristic of halides whose solvolysis is known to proceed *via* the S_N2 pathway. In general, an m value of 0.5 can be taken as an approximate indicator of an S_N1/S_N2 mechanistic borderline in solvolysis reactions of this kind.

The major defect of the Grunwald–Winstein treatment is that it is limited in its scope. It has been applied to reactions other than halide solvolysis, but is in general restricted to those reactions for which the major contribution to the rate-limiting step is of the form:



13.6.3 Dimroth's E_T parameter

There have been several other attempts to define solvent polarity parameters, among the more successful being those related to *solvatochromic shifts*: the shift in wave-length/frequency of a band in the spectrum of a suitable absorbing species resulting from its interaction with the molecules of a series of different solvents. Particularly large shifts were observed with the zwitterion (51),



(51)

whose absorption maximum was found to vary between 450 and 1000 nm, depending on the solvent: its solution being yellow in MeOH, red in Me_2CHOH , and blue in CHCl_3 ! Dimroth took as a measure of solvent polarity, E_T : the excitation energy (ground \rightarrow excited state) in kcal mol^{-1} at the absorption maximum in that solvent. The justification for E_T is that the ground state of (51) is

very much more polar than the excited state to which it gives rise, and so will, of the two, be stabilised to a much greater extent by polar solvents. Assuming that the effect of solvent variation on the energy level of the excited state is only small, then the varying values of E_T observed will be a measure of the relative stabilisation of the ground state (51), and hence of the relative polarity of the solvent involved; E_T rising as the stabilisation, and hence solvent polarity, increases:

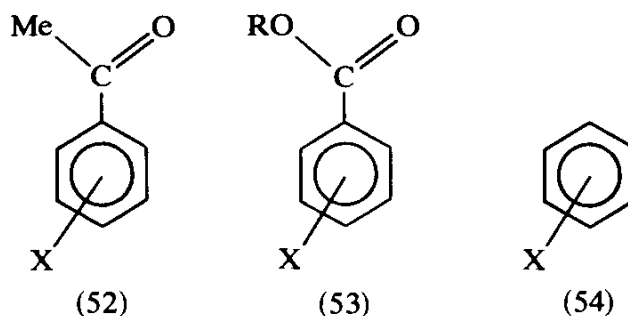
Solvent	E_T	Y_A
H ₂ O	63.1	+3.49
HCONH ₂	56.6	+0.60
aq. EtOH (20% H ₂ O)	53.7	0
aq. Me ₂ CO (20% H ₂ O)	52.2	-0.67
MeOH	55.5	-1.09
EtOH	51.9	-2.03
Me ₂ CHOH	48.6	-2.73
Me ₃ COH	43.9	-3.26
CHCl ₃	39.1	—

Values of Y_A (cf. p. 390) for the same range of solvents are included for comparison; by and large the E_T parameter is the more successful of the two, and has somewhat wider application.

13.7 SPECTROSCOPIC CORRELATIONS

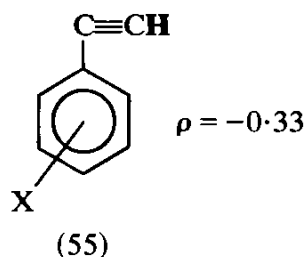
We have discussed at some length correlation of the chemical properties of X-substituted molecules with σ_X —the polar substituent constant for X—and it is pertinent to enquire whether similar correlations can also be established between σ_X and their *physical* properties, among which spectroscopic data constitute a readily accessible example.

There have been many attempts to correlate σ_X with the frequency and/or intensity of bands in the i.r. spectra of X-substituted aromatic species. Among the most successful have been with the frequency of the C=O band in (52) and (53), and with the intensity of the 1600 cm⁻¹ ring vibration in (54):



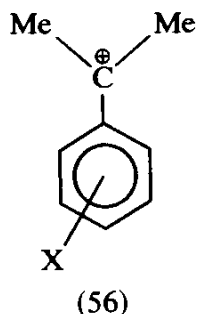
We might well expect to find reasonable correlations of σ_X with chemical shift, δ , data (cf. p. 18) from n.m.r. spectra, which do, after

all, reflect the degree of electron shielding or de-shielding at the relevant atom. In fact, correlation of δ data for ^1H with σ_{X} has not been very impressive except, as with (55),

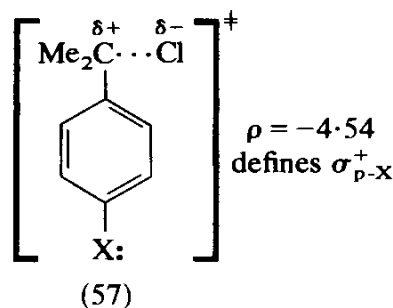
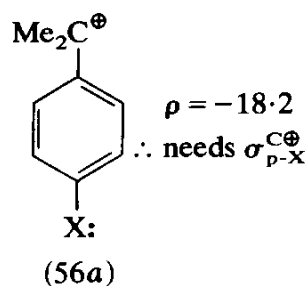


where the relevant proton is fairly remote from the substituted benzene ring.

However, an atom somewhat heavier than ^1H might well be less susceptible to the perturbations that may disturb the latter; as, for example, ^{13}C which also generates an n.m.r. spectrum. Thus the 2-arylpropyl(cumyl) carbocations (56; produced from the corresponding tertiary alcohols in 'super acid' $\text{—SO}_2\text{ClF/FSO}_3\text{H/SbF}_5\text{—}$ solution, cf. p. 181),



showed a good straight line correlation of the ^{13}C chemical shift difference (for the carbocation carbon: $\delta\text{C}_{\text{H}}^{\oplus} - \delta\text{C}_{\text{X}}^{\oplus}$) with $\sigma_{\text{m-X}}^+$, but *not* with $\sigma_{\text{p-X}}^+$. Correlation of the shift differences for the *p*-substituted carbocations required enhanced *p*-substituent constants, $\sigma_{\text{p-X}}^{\text{C}\oplus}$, reflecting the much more powerful 'through conjugation' with *p*-X in the fully formed carbocation (56a), as compared with that in the only partly formed carbocation (57) in the T.S. for cumyl chloride solvolysis—the standard reaction that was chosen (p. 357) to define $\sigma_{\text{p-X}}^+$:



13.8 THERMODYNAMIC IMPLICATIONS

It is perhaps interesting, in view of the very considerable success of Hammett plots, to say a word finally about the thermodynamic implications of linear free energy relationships in general. We have already mentioned (p. 359) the relationship between free energy change, ΔG , and $\log k$ or $\log K$; and each ΔG term is, of course, made up of an enthalpy, ΔH , and an entropy, ΔS , component:

$$\begin{array}{ll} \text{Equilibrium} & \underline{\Delta G}^\ominus = -2.303 RT \log K \\ \text{constant:} & \underline{\Delta G}^\ominus = \Delta H^\ominus - T\Delta S^\ominus \end{array}$$

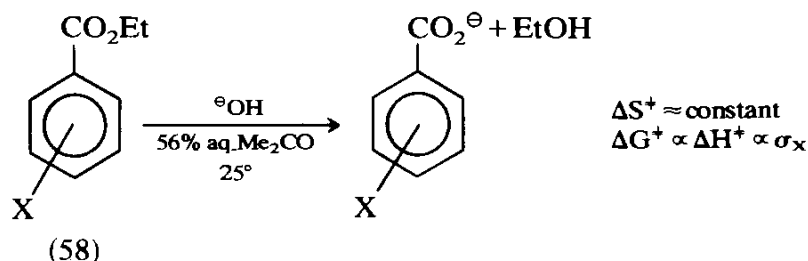
$$\begin{array}{ll} \text{Rate} & \underline{\Delta G}^\ddagger = -2.303 RT \log k \frac{h}{k'T} \\ \text{constant:} & \underline{\Delta G}^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger \end{array}$$

$$\left[\begin{array}{l} k' = \text{Boltzmann's constant} \\ h = \text{Planck's constant} \end{array} \right]$$

Looking back at one of our earliest examples—Fig. 13.3 (p. 361) in which $\log K$ for the ionisation of ArCO_2H is plotted against $\log k$ for the base-catalysed hydrolysis of ArCO_2Et —the straight line implies that there is also a linear relationship between the ΔG^\ominus values for the former reaction and the ΔG^\ddagger values for the latter. Such a straight line relationship between these two series of ΔG terms is to be expected only if, for *each* series, one or other of the following conditions is satisfied:

- (1) ΔH is linearly related to ΔS for the series
- (2) ΔH is constant for the series
- (3) ΔS is constant for the series

Any of these conditions constitutes an extremely stringent limitation, and there has always been some doubt expressed over the extent to which any one of them is indeed satisfied in reactions which nevertheless give quite good straight line Hammett plots: thereby making the linear relationships that are observed all the more mysterious! Examples are, however, known that can indeed be shown to conform to one or other of the above conditions. Thus for the base-induced hydrolysis of the esters (58),



ΔS^\ddagger is found to be virtually constant—condition (3) above—and ΔG^\ddagger , or ΔH^\ddagger , is thus found to be proportional to σ_{X} . Not altogether surprisingly, no convincing example is known in which condition (2)

is met, but condition (1) might well be expected to be one that is most frequently satisfied. Interestingly enough, doubt has in the past been expressed as to whether even the standard, reference reaction—the aqueous dissociation of *m*- and *p*-substituted benzoic acids in water at 25°—satisfied this condition.

A major obstacle to deciding the truth or otherwise of this assertion about benzoic acid ionisation has been the experimental difficulties involved in making the necessary measurements. The solubility of the acids in water is pretty low, and their ΔH^\ominus values are very small, with consequent imprecision in, and unreliability of, the results so obtained. Relatively recently, however, ΔG^\ominus , ΔH^\ominus and ΔS^\ominus have been redetermined, with great precision, for a series of ten *m*- and *p*-substituted benzoic acids. Using these data, stringently linear plots were obtained for ΔH^\ominus against ΔS^\ominus , for ΔG^\ominus against ΔH^\ominus , and for ΔG^\ominus against ΔS^\ominus . So it looks as though Hammett was on to a good thing after all when he made his choice of standard, reference reaction in the first place!

It is important, however, to remember that what theoretical interpretation there has been of the Hammett equation has come from circumstantial evidence rather than by rigorous proof. It remains an empirical relationship and, to that extent, there is no point in even trying to evaluate σ_X and ρ to several places of decimals. The sort of information we need, as an aid to the elucidation of reaction pathways, is of an 'order of magnitude' kind: such things as whether ρ is +ve or -ve, whether its value is large or small, whether there are noticeable deviations from linearity in plots of σ_X against $\log k_X$ and, if so, of what kind. This also raises the question of multi-parameter equations, not so much of their general validity but of their actual usefulness. While they are certainly of considerable interest to physical organic chemists, it is more doubtful—so far as practising organic chemists in general are concerned—whether the extra labour, necessarily involved in evaluating all these further parameters, is repaid by the quality of the additional information that is thereby gained: you pay your money and you take your choice!

Having said all that, it is equally important to remember that the number and variety of useful correlations to which Hammett plots have given rise is quite astonishing, particularly when we consider the simplicity and convenience of the approach. Indeed, linear free energy relationships in general constitute a testament to the theoretical utility of concepts that are purely empirical in their genesis!